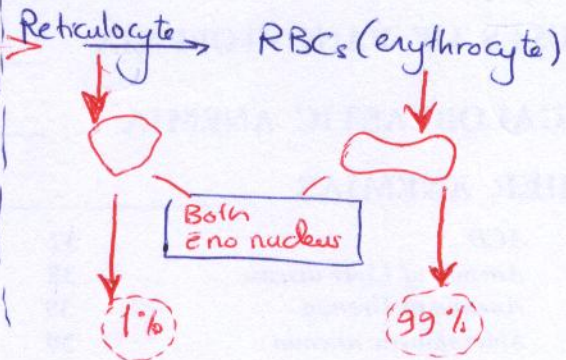
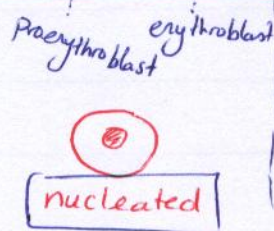
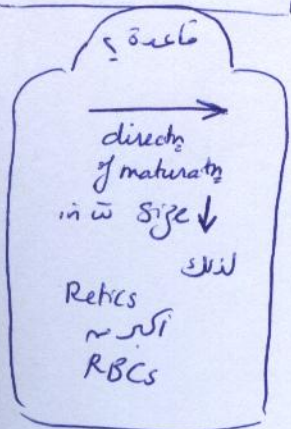
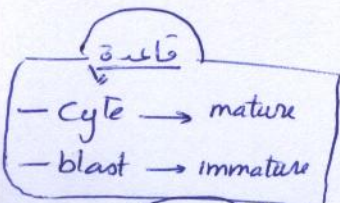
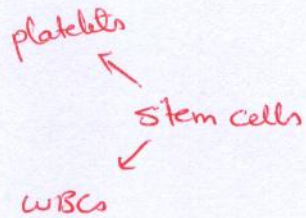
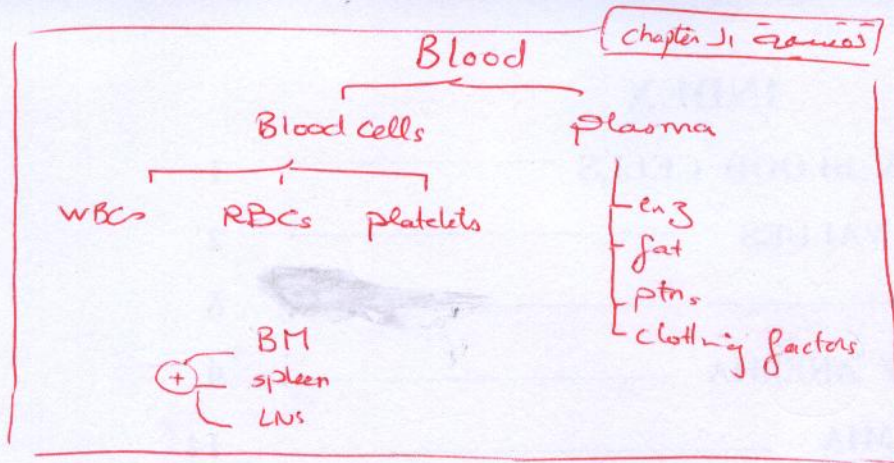


VISIT...

LANZAROTE
Caliente.COM



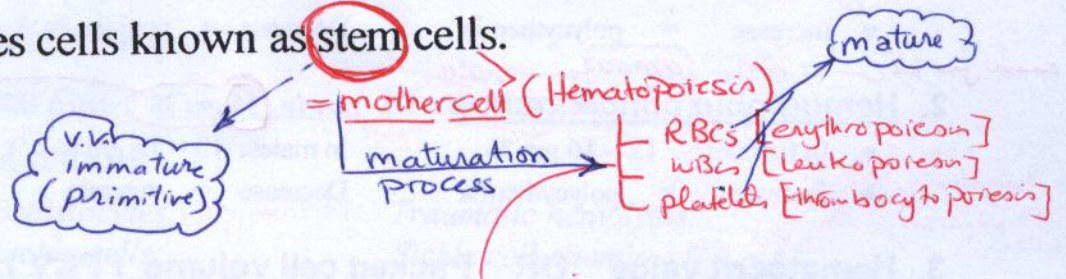
Skull

vertebrae
ribs

Pelvic (hip) bone
proximal part of long bone

BONE MARROW

- It is a spongy material in the centre of some of our bones.
- It produces cells known as stem cells.



STEM CELLS

- Immature cells that develop into 3 different types of blood cells.
- * maturation (differentiation) → (needs Fe, F.A., B₁₂) → if ↓ (slow maturation)
- * Proliferate (multiplication) → أسرع انقسام (Proliferate) → Blood cells (خلايا الدم)

BLOOD CELLS

- Red blood cells: Hb carry oxygen to all cells in the body. (if Hb ↑ → حمراء زكية → Hyperchromic)
- White blood cells: fight infections and form part of our immune system.
- Platelets: help the blood to clot, to prevent bleeding. (plug)

بعض الخلايا
infectious
بعضها تقاوم
Cancer cells



eg: Hb: 9
Ht: 30
RBCs: 3 million } = anemia
MCHC 25 = hypochromic
MCV 75 = microcytic } 4 diagnoses only

فحص
و 10% اسنان
Clinical Pathology

NORMAL BLOOD VALUES

A) RED BLOOD CELLS

1. Red cell count: ^{menstruata}

- In females: 4.5 - 5 millions
- Increase = polycythemia

nearly 5 millions / cmm

In males: 5 - 5.5 millions.

Decrease = anemia.

androgens (→ erythropoietin)

2. Hemoglobin concentration:

- In females: 12 - 16 gm %
- Increase = polycythemia

nearly 15 gm %

In males: 13 - 17 gm %.

Decrease = anemia.

100 CC.
= 100 ml
= 1 dL
نحس الليتر
Hb فيه
15 gm
هو برينه يخاص
بالجرام مش الليتر

3. Hematocrit value OR Packed cell volume (PCV):

- It is the volume of packed red cells in 100 ml of blood.

- In females: 36 - 48 %

- Increase = polycythemia

In males: 40 - 52 %.

Decrease = anemia.

4. Red cell indices:

a) Mean Cell Volume (MCV):

- It is nearly 90 CM.

- In anemia: if MCV < 80 → microcytic anemia.
- if MCV 80 - 100 → normocytic anemia.
- if MCV > 100 → macrocytic anemia (megaloblastic)

1L = 1000 ml
1ml = 1000 micro
1uL = 1000 nano
1 nano = 1000 Pico
1 Pico = 1000 Femto

Cubic micron / FL = Femto litre

b) Mean Cell Hemoglobin Concentration (MCHC):

- It is the average hemoglobin concentration in the red cells.

- It is nearly 34 gm / dL.

- In anemia: if MCHC < 30 → hypochromic anemia.
- if MCHC 30 - 35 → normochromic anemia.
- if MCHC > 35 → hyperchromic anemia.

$$\frac{Hb}{Ht} = \frac{15}{45\%} = \frac{15}{45} \times 100$$

$$= \frac{15 \times 100}{45} = \frac{1500}{45} = 33.3333$$

(30 - 35)

↓ ↓ ↓ (Hb) ↓ ↓ ↓ (Ht)
↓ ↓ ↓
↓ ↓ ↓

5. Reticulocyte count:

(normally: 0.5 - 1.5 %)

1% = 50,000

نمينا 1% مركز

- Reticulocyte:** a young immature RBC newly released from the BM.
- Reticulocyte count:** reflects the rate of RBC production in the BM.
- Reticulocytosis:** ↑ reticulocyte count occurs in cases of over active BM:

- Hemolytic anemia.
- Acute hemorrhage.
- Anemia under ttt.
- Recovery from BM suppression.

- Reticulocytopenia:** ↓ reticulocyte count, occurs in cases of suppressed BM:

- Aplastic anemia.

after Antithyroid (causes ↓ in cell lines)

W treat thyrotoxicosis

if stop drug: BM works

لازم
بعد
التنوع
الزيف
Retic
تزيد
ودي
خلالة
كويصة

نزيف جوة
نزيف برة

مستجيب
على
عوامل

حاجة واحدة بس

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6. Red cell diameter:

- The Mean Cell Diameter (MCD) is 7.2 Microns.
- Microcytosis = less than 7.2 Microns.
- Macrocytosis = more than 7.2 Microns.
- Anisocytosis = variations in size.

Caused by
* Prosthetic valve

7. Red cell morphology:

- Normal red cell:
- Abnormal red cell:

- Schistocytes: (fragmented)
- Sickle cells:
- Spherocytes:
- Target cells:
- Teardrop RBCs:
- Howell-Jolly bodies:
- Poikilocytosis:

remnants
of nuclear
material

Biconcave disc.

Traumatic hemolysis.

Sickle cell anemia.

Hereditary Spherocytosis.

Thalassemia.

Idiopathic myelofibrosis.

Hyposplenism.

Variable shapes.

diagnosed
mainly by Hb
electrophoresis

by osmotic
fragility test

by Hb
electrophoresis

deposited
Hb f

v. non specific

B) WHITE BLOOD CELLS

1. Total leukocytic count (TLC):

- Increase = leukocytosis

4,000 – 11,000 / cmm.

Decrease = leukopenia.

2. Differential leukocytic count:

- Neutrophils: 50 – 70 %
- Eosinophils: 2 – 5 %.
- Basophils: 0 – 1 %.
- Lymphocytes: 20 – 40 %.
- Monocytes: 2 – 8 %.

= polymorph
= granulocytes

Band
(Staff : Segmented = 1 : 10)



immature
1



N: 3-5 segments
mature
10

if spleen can't
destroy
abn. cells
properly
↓
Remnants of
nuclei

Differential neutrophil count

- Shift to the left: ↑ Staff in overactive BM (bacterial infections).
- Shift to the right: ↑ Segmented in delayed BM (megaloblastic anemia).

Schilling

band

جانب

نيل خلايا
في كثافة

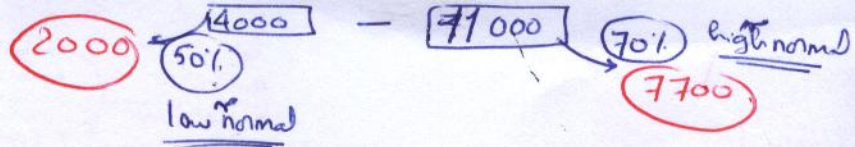
high normal ~ 1st segments ~ 3-5

→ 6-7-8 segments

↓ F.A, B₂

abnormally
prolonged
maturation time

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more segmented



Neutrophilia (> 7500 / cmm)

a) Physiological: exercise, emotional stress, pregnancy.

b) Pathological:

- **INFECTIONS** especially BACTERIAL INFECTIONS.
- **INFLAMMATIONS** e.g. collagen diseases as SLE & RA.
- **Iatrogenic:** e.g. corticosteroids.
- **Hemorrhage.**
- **Hemolysis.**
- **Trauma & burns.**
- **Tissue injury:** e.g. myocardial infarction.
- **Malignancy:** e.g. carcinoma, or blood malignancies.
- **Metabolic:** e.g. DKA, uremia.

Neutropenia (< 2000 / cmm) = Agranulocytosis = Granulocytopenia

- ① **Bone marrow aplasia:** see "aplastic anemia".
- ② **Bone marrow infiltration:** (Myelophthisic anemia)
3. Immunological: autoimmune diseases.
4. Infections: Viral infections, TB, Typhoid.
- ⑤ **Megaloblastic anemia.**
- ⑥ **Hypersplenism.**

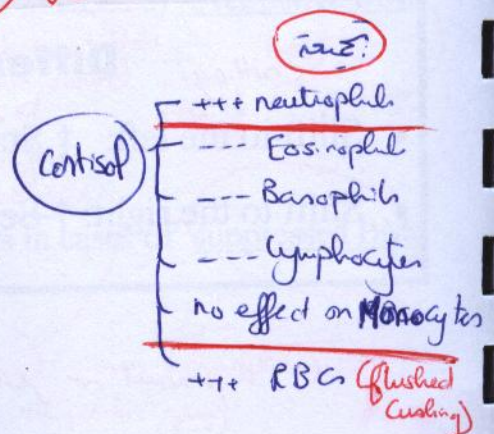
Eosinophilia

- ① **Allergic disorders:** Bronchial asthma, allergic rhinitis, urticaria.
- ② **Parasitic infestations:** Toxocara, Schistosoma, Filaria, Ankylostoma
3. Skin diseases: Allergy, Psoriasis.
4. Immune: PAN, RA.
5. Malignancy: Eosinophilic leukemia, Hodgkin's disease.
6. Miscellaneous: Loeffler's syndrome, Addison's disease.

Eosinopenia

1. **A**cute infections.
2. **B**urns.
3. **C**ushing's syndrome, Corticosteroid therapy.

↑ cortisol



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Basophilia

1. **M**alignancies of the blood: e.g. leukemia.
2. **M**yoedema.

Basopenia

1. Allergy.
2. Corticosteroid therapy.
3. Hyperthyroidism.

= Persistently Zero

الحمى
يعنى لو واحد
Basophils
عنده كانت ساقى zero
لا تخاف على راسها
بعد اسبوعين تتلاشى لا فية
بها عرقا ما تكون طول الوقت zero

Lymphocytosis

1. Acute **VIRAL** infections: Hepatitis, HSV, IMN, CMV.
2. Chronic BACTERIAL infections: **TB**, Brucellosis, Syphilis.
3. Lymphomas: especially Lymphocytic lymphomas. **Non Hodgkin**
4. Lymphatic leukemias: acute & chronic.

Lymphopenia

1. Immunodeficiency diseases. $\left. \begin{matrix} \downarrow T \\ \downarrow B \end{matrix} \right\} \text{lymphocytes}$
2. DRUGS: Immunosuppressive drugs & Corticosteroids.
3. Lymphomas: especially Hodgkin's disease.
4. Cushing's syndrome.
5. Malnutrition & Malabsorption.

لنفوق
Lymphoma
قل
Penia
or
cytosis
تقول اللينفوق
Penia ← HL
cytosis ← NHL

Monocytosis

1. Infections: Brucellosis, Typhoid, TB, Syphilis, SBE, **IMN**.
2. Malignancy: Monocytic leukemias, Hodgkin's disease. (الاشهر)
3. Miscellaneous: Collagen diseases, Sarcoidosis.

Monocytopenia

1. Aplastic anemia.
2. Infections: HIV.
3. Immune: SLE.
4. Malignancy: CLL.

C) PLATELET COUNT

- Normally: 150,000 – 400,000 / cmm.

Thrombocytopenia $\leftarrow < 150,000$ $> 400,000 \Rightarrow$ Thrombocytosis
thrombocythemia

ANEMIA

نفری +
Clinical
Hemolytic A.

DEFINITION

1. Reduction in:

- RBCs • Red cell count
- Hb • Hemoglobin concentration
- Ht • Hematocrit value

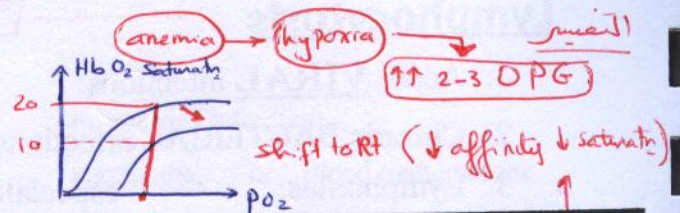
lab. not Clinical diagnosis

Reduction of the O₂ carrying capacity of the blood.

THEREFORE:

2. Reduction in:

- O₂ delivery to the tissues.



COMPENSATORY MECHANISMS IN ANEMIA

Several compensatory mechanisms occur to maintain tissue oxygenation:

1. Increased O₂ delivery to the tissues:

through

- o Increased cardiac output. (anemia → HOC → ↑ CO Failure)
- o Peripheral vasodilatation. (due to hypoxia)
- o Reduced affinity of Hb to O₂.

2. Increased erythropoietin production:

to ↑ red cell production in the BM.

3. Increased plasma volume:

to maintain the total blood volume normal.

1 ↓ viscosity
↑ RBC → CO
2 hypoxia
VD
3 hypoxia
↑ sympathetic
↑ HR

$$\uparrow CO = \uparrow HR \times SV$$

hypoxia → renal renin → Aldosterone → Na⁺ H₂O retention
hemodynamics ↓ → volume of circulation ↓

FACTORS AFFECTING THE SYMPTOMS OF ANEMIA

1. Speed of onset:

- Rapidly progressive anemia causes more symptoms than anemia of slow onset, because there is less time for compensatory mechanisms to occur

2. Severity of anemia:

- Mild anemia may be asymptomatic. (12, 13) while 7 g/dl (severe)

3. Senility:

- Symptoms are more severe in the elderly due to: impaired cardiovascular compensatory mechanisms in the elderly.

15 15
↓ ↓
7 7
↓ ↓

CLASSIFICATION

I. ETIOLOGICAL CLASSIFICATION

A) Decreased red cell production:

1. Decreased proliferation (Hypoproliferative anemia)

- Aplastic anemia.
 - Myelophthisic anemia. *Pathic*
 - Anemia with organ failure:
 - Renal failure, liver failure, endocrinal failure.
- phthisis = T.B.*
لأنهم ادركوا الكسوف
كانت عليه TB
دخلت B.M. ووقف
عن ذلك من الغرغرة التي يفتح

2. Decreased maturation (Dyshematopoietic anemia)

- Iron deficiency anemia.
 - Megaloblastic anemia: *B12* or *folic acid* deficiency.
 - MDS. *Myelo Dysplastic Syndrome*
 - Sideroblastic anemia
- ↓ Fe*
↓ B12 ↓ FA
maturate = hematopoietic

B) Increased red cell destruction:

- Hemolytic anemias. *eg thalassemia*

C) Increased red cell loss:

- Acute post-hemorrhagic anemia.

II. MORPHOLOGICAL CLASSIFICATION

A) Microcytic hypochromic anemia:

- 1. Iron deficiency anemia.
 - 2. Thalassemia. (hemolytic)
 - 3. Sideroblastic anemia.
 - 4. Anemia of chronic disease (ACD). ✓✓✓
- < 80*

B) Normocytic normochromic anemia:

- 1. Aplastic anemia.
 - 2. Myelophthisic anemia.
 - 3. Anemia with organ failure.
 - 4. Hemolytic anemia.
 - 5. Acute post-hemorrhagic anemia.
 - 6. Anemia of chronic disease (ACD). ✓
- 80-100*

C) Macrocytic anemia:

- 1. Megaloblastic anemia: *B12* or *folic acid* deficiency.
 - 2. Miscellaneous: Alcohol, liver failure, reticulocytosis, Myxoedema, MDS.
- > 100*

- ① ↓ F.A. absorption
- ② ↓ F.A. metabolism

① ↓ storage of *B12* & *F.A.*
خلايا حبيبية

② obstructive jaundice (P.S.)
 due to thickening of RBCs membrane by deposited cholesterol p.L.
 due to their retention from obstructive

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MANIFESTATIONS OF ANEMIA

فقر الدم
anemia

I. GENERAL MANIFESTATIONS OF ANEMIA

Symptoms

1. General:

- Easy fatigue, lassitude, stunted growth *in children with chronic severe anemia.*

2. CVS:

- Palpitation, exertional dyspnea.
- Precipitation of angina, precipitation of **HF** (high cardiac output HF).
- Intermittent claudications in severe cases.

3. Neurological:

- Headache, dizziness, blurring of vision, syncope.
- Lack of concentration.
- Numbness & tingling: of feet & hands.

4. Genital:

- FEMALE: Menstrual irregularities, MALE: impotence.

Signs

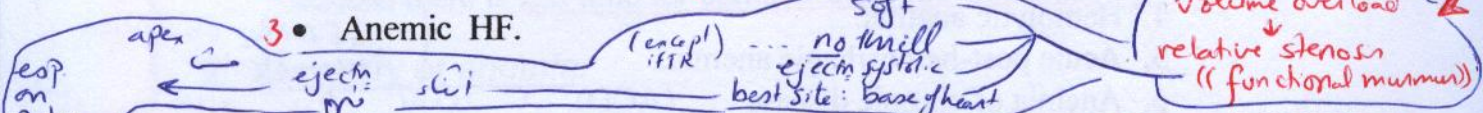
- Pallor:** best detected in: *mm of mouth & conjunctiva, palmar creases, nail folds.*

- Hyperdynamic circulation:**

- Pulse: Tachycardia & big pulse volume.
- Heart: ~~HR~~ Accelerated heart sounds, S₃, hemic murmurs.
- In severe cases: High cardiac output **HF**.

- Oedema of LL:**

1. Hypoxia: which increases the capillary permeability.
2. Salt & water retention. (Aldosterone ↑ by renal ↑)
3. Anemic HF.



II. SPECIFIC MANIFESTATIONS OF ANEMIA

- These are manifestations related to the specific cause of anemia "see later".

eg: Fe def. anemia:

1. if HF → S₃ (flabby)
2. even if no HF → S₃ (vol. overload)

loss
GIT
Ankylosoma & Angiodysplasia

واحد من أهم مواضيع هذا الكتاب
نظرة سريعة

IRON DEFICIENCY ANEMIA

أهم جانب
Investing Ht

DEFINITION

- **Iron deficiency** is defined as: a decreased **total** iron body content.
- **Iron deficiency anemia** occurs when: iron deficiency is sufficiently severe to diminish erythropoiesis and therefore cause the development of anemia.
- **It is the most common type of anemia.**

ETIOLOGY

1. Decreased intake of iron:

- Infants: because iron content of milk is low.
- Elderly: and poor people.

2. Decreased absorption of iron:

- Achlorhydria: e.g. atrophic gastritis, gastrectomy, cancer stomach.
- Diet: ↑↑ phosphate & phytate (cereals) or tannate (tea) or oxalates.
- Pica: = Perverted appetite. Ingestion of unusual substances such as clay → ↓↓ iron absorption.
- MALABSORPTION SYNDROME. → ↓ in other nutrients

3. Increased demand for iron:

- Females in child-bearing period: pregnancy & lactation.
- Growth periods: infancy & adolescence.

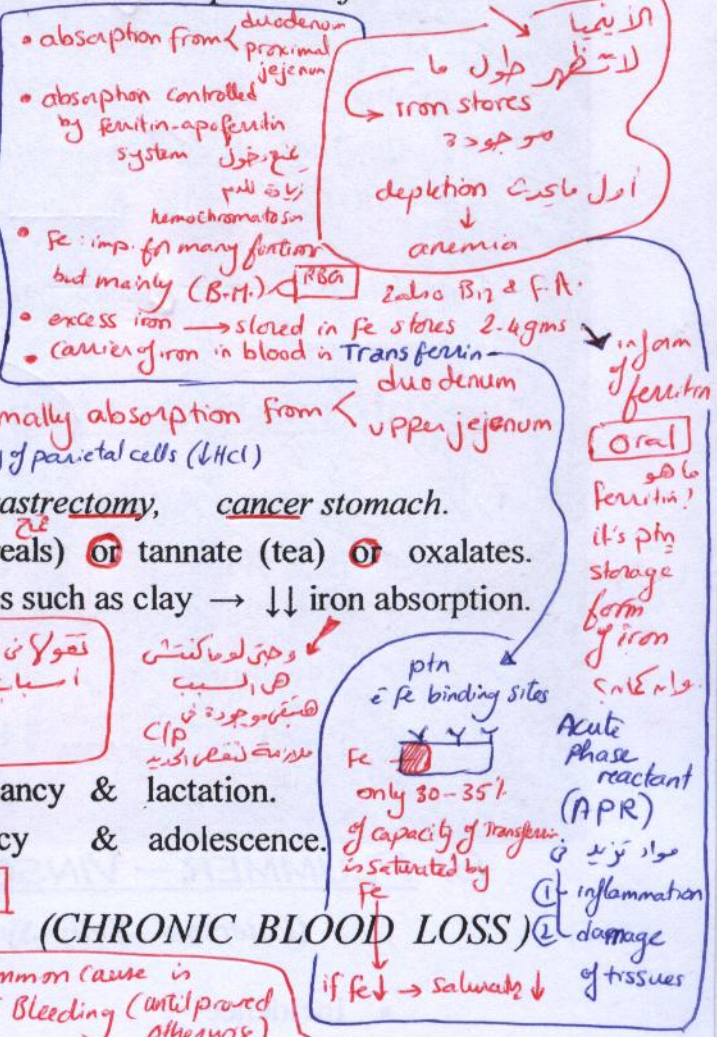
4. INCREASED LOSS OF IRON:

GIT:

- Oesophagus: varices,
- Stomach: peptic ulcer,
- Intestine: Ancylostoma infestation, Angiodysplasia, IBD, piles,

Iron deficiency in an adult male means GIT blood loss until proven otherwise

- **Recurrent bleeding:** epistaxis, hematuria, bleeding from wounds, menorrhagia.
- **Repeated blood donation.**
- **Hemorrhagic blood diseases.**
- **Hemoglobinuria.**



النزف
أهم
أسباب
Oral

دهش نريف
نرف عام

CIP
1. massive rapid acute bleeding (rare)
2. Mild Slow Bleeding (common)

vascular malformation in GIT
abnormal: dilated, Fragile easily Bleeding
Causes: degenerative changes (aging)
sites: any part of GIT but most

PICA
Post infarction cerebellar A.

due to Intravascular hemolysis & hemolytic crisis

CLINICAL PICTURE

1. General manifestations of anemia: "see before".

اشرحه كالمه

2. Manifestations of iron deficiency: → Fe needed for cells to regenerate (aroid atrophy)

- **Mouth:** Angular stomatitis (Cheilosis).
- **Tongue:** Atrophy of tongue papillae. = Atrophic glossitis = glazed tongue
- **Nose:** Atrophy of nasal mucosa + bad smelling discharge (**Ozena**).
- **Appetite:** Perverted appetite ^{يعتبر انظر من لب} (Pica).
- **Nails:** Brittle, flattened, loss of luster + Spooning (**Koilonychia**).
- **Spleen:** Mild splenomegaly to provide extramedullary hematopoiesis (in 10 % of the cases).

3. Manifestations of specific types of iron deficiency:

A) ANCYLOSTOMA ANEMIA:

- Loss of iron: ↓ Features of iron deficiency anemia including Pica.
- Loss of proteins: ↓ Hypoalbuminemia. due to PLE (protein losing enteropathy)
- Abdominal pain, Alternating diarrhoea & constipation.
- Blood: inflammatory by parasites Eosinophilia. ++ Allergy parasite
- Stools: Ancylostoma ova.

B) PLUMMER - VINSON SYNDROME.

(Paterson - Kelly Syndrome) (لا تعرف)

- Incidence: usually occurs in middle aged females.

- Features of iron deficiency anemia: especially,

Stomatitis, **Spooning**, **Splenomegaly**.

- **DYSPHAGIA:** due to oesophageal web (desquamating epithelial cells), which:

- may obstruct the oesophagus.
- may be complicated by: post-cricoid carcinoma.
- may appear in Ba swallow as a: post-cricoid web.

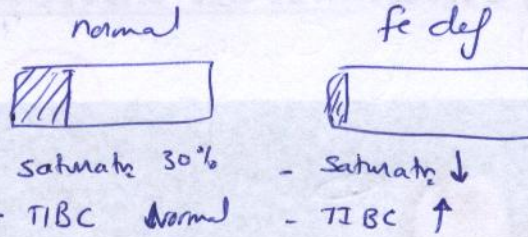
be def + esophagus

فيه ناس يقول
web nit
↓
رونا خط
فيه ناس يقول
web عمل

oral

TIBC ? what does it measure ?

measures amount of fe needed to fully saturate Transferrin



oral ¹⁰⁰⁰

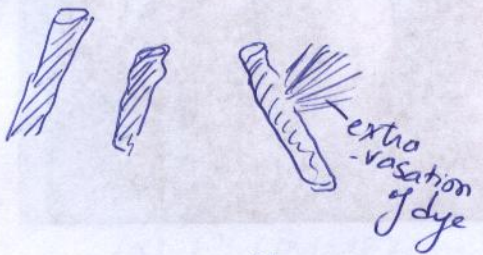
FEP

Free Erythrocyte protoporphyrin

خرج داخل RBC

Angiography:

أشعة مائة زئبقية
"dye"



if rapid massive bleeding

اما فقط خفيفة جدا لا تظهر



الكل ألون RBC

بلون radioactive والقدر بكاميرا
gamma camera

Iron + protoporphyrin

enz

Heme

(+ globin)

Hb

• if iron ↓

protoporphyrin accumulates

Sensitive test (in all fe deficiency)

but not specific (not only in fe deficiency)

• also if eng inhibited by lead

• also if sideroblastic anemia iron use decreases

أشعة مائة زئبقية و خفيف على Technique
وأعمل scan بلا X-camera فاعذر القدر

INVESTIGATIONS

I. For diagnosis of iron deficiency anemia:

1. CBC: "Features of microcytic hypochromic anemia"

RBCs:

- Decreased: Red cell count, Hemoglobin level, Hematocrit value.
- Decreased: MCV & MCHC.

WBCs:

- Usually normal.
- Eosinophilia is present in Ancylostoma infestation.

Platelets:

- Usually normal.

اشبع
كاملا
normal
value

anemia

microcytic
hypochromic

2. Bone marrow examination:

- Erythroid hyperplasia. → non specific (present in any anemia)
- Decreased iron stores in macrophages. → aplastic (present in any anemia)

3. Evidence of iron deficiency:

iron profile

- Serum iron, ferritin, transferrin saturation: decreased.
- TIBC: increased.
- FEP: increased.

Total Iron Binding Capacity

aplastic
leukemia

Bm.
دورقوى

II. For diagnosis of the cause:

1. Stool examination:

- For occult blood
- For Ancylostoma ova.

(precautions). detects Hb in stools
لا تكون نزيهه خفيف لا يغفل عنه لبار

2. Investigations for GIT hemorrhage:

- Endoscopies: oesophagoscopy gastroduodenoscopy, colonoscopy.
- Barium studies: Ba swallow, Ba meal, Ba enema.

- Angiography: is useful in cases of rapid bleeding.

RADIO-ISOTOPE BLEEDING SCAN:

- Radio-isotope scanning of the abdomen after IV injection of Technetium is useful when active bleeding is too slow to be detected by angiography.

- highlighten RBC

& minor

Cardio
• CAD Tech. Thallium
• P. Emb.
Albumin Xenon
White Knight Love
inched ILD

اشبع
وساظر

1) يمنع اللحوم الحمراء في الشاي 2) أيام على الأقل
3) لا يفضل استئصال بالقرص 2-3 أيام
2) لا تأخذ دواء 2-3 أيام
Aspirin
NSAID
Cortisol
gastrolin
تأثيره يقل شدة

مفيد فقط في هذه الحالات
والألو قليل ارتطاب

oral also in $\uparrow$ HCl $\rightarrow$ peptic ulcer
used in $\downarrow$ HCl $\rightarrow$ Zollinger Ellison syndrome (gastrinoma) طالع pancreas

3. Investigations for hemostatic disorders:

- See later. Bleeding time P.T APTT
Clotting time T.T

4. Investigations for malabsorption syndrome:

- Refer to GIT. Urinary-D-xylose test احد

5. Gastric function tests:

- To detect achlorhydra. Pentagastrin stimulation test

DIFFERENTIAL DIAGNOSIS

- Causes of: Microcytic anemia:

1. Iron deficiency anemia.
2. Thalassemia.
3. Sideroblastic anemia.
4. Anemia of chronic disease

اشح scheme
الترتو
كل من
most imp.
arterial
leach
(ACD)

1st measure HCl basal level (fasting)
2nd stimulate parietal cells to produce HCl
 $\rightarrow$ (persistent $\downarrow$ HCl)
(normally: $\uparrow$ after stimulation)

TREATMENT

I. Specific TTT

A) TTT of the underlying cause: e.g. ttt of Ancylostoma infestation.

B) Replacement therapy:

- **AIM**

1. To correct anemia: i.e. to restore the normal Hb level.

1) monitor by $\rightarrow$ (Hb $\uparrow$ about 1 gm % weekly until normal levels are restored)
2) monitor by $\rightarrow$ (Reticulocyte count begins to $\uparrow$ within 5 days of starting ttt)

Causes of impaired response: (persistent)

- o Presence of persistent blood loss.
- o Associated $\downarrow$ in Hb synthesis.
- o Noncompliance to ttt.

Fe $\downarrow$ نقص الحديد
F.A. 8 B12
malabsorption

2. To replenish the iron stores: i.e. to provide stores of at least $\frac{1}{2}$ to 1 gm of iron.

(Continuous ttt for 6 months after correction of anemia will achieve this)

ارتفاع 9 $\rightarrow$ 10 $\rightarrow$ 15 خلال وقت العلاج
هذا الكلام غلط جدا لوزن تستمر 6 شهور

White Knight Love
1 gm

METHODS

1. Iron - rich diet:

- Meats: beef, chicken, fish.
- Vegetables: leafy greens, legumes, peas, etc....
- Others: pasta, rice, yeast.

hemolytic jaundice
الوجع في البطن
jaundice

Fe oral
melena (tarry)
hemolytic anemia

2. Iron preparations:

a) Oral iron:

- Preparations: ferrous sulphate, ferrous gluconate, ferrous fumarate.
- Dose: 300 mg tds.

Side effects:

- GIT irritation: anorexia, nausea, vomiting, abdominal pain, constipation.
- Dark stools.

b) Parenteral iron:

- Preparations: Iron dextran (IV), or Iron sorbitol (IM).
- Dose: 100 mg / day IV or IM.

Side effects:

- Local: pain, inflammation, abscess formation, thrombosis. (superficial)
- General: fever, flushing, headache, hypotension, arthralgia, anaphylaxis.

Indications:

- Intolerance of oral iron.
- Malabsorption syndrome.
- Rapid iron loss.
- GIT disorders that may be aggravated by oral iron:
e.g. peptic ulcer, IBD.

irritant مادة
على GIT و يمكن ان يحترق

أفضل أن يعطى الحقن
في أوقات الإفطار
أو بعد الإفطار

oral iron

غير مفيد
غير سريع
يرجع
به لانه
irritant

Antihistaminic
Adrenaline
Cortisol.

allergy
لازم في الحساسية
ولو حصلت أدل
وكانت عنده يحصل
بعد كده
رغم ان حاجه اسعاف
اختار حشمت

II. Transfusion therapy:

- Packed red cell transfusion may be needed in cases of severe anemia:

- Hemoglobin: < 7 gm %.
- Marked symptoms of anemia.
- Anemic HF.

not whole blood But
only packed RBCs to
avoid vol-overload

III. Symptomatic TTT:

- e.g. ttt of anemic HF.

Diuretics
Digitalis

هو ان نأخذ حبة Fe
وكانت يتغير عنه
Hf.

Clinical
Long
Short

se
r

HEMOLYTIC ANEMIA

DEFINITION

- It occurs due to: premature destruction of the RBCs → short life span of RBCs.
- It occurs when: BM activity cannot compensate for the destroyed RBCs.
- Hemolysis may be: intravascular or extravascular.

ETIOLOGY

I. CORPUSCULAR CAUSES

1. Membrane defects:

- Hereditary spherocytosis (HS).
- Paroxysmal nocturnal hemoglobinuria (PNH).

2. Hemoglobin defects: "Hemoglobinopathies"

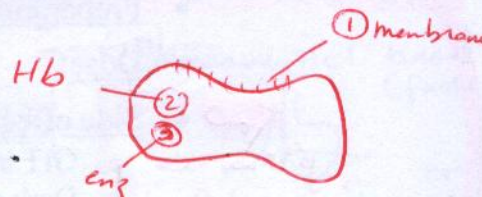
- Thalassemias.
- Sickle cell anemia.
- Rare types: Hb C, Hb D, Hb E.

3. Enzyme defects:

- Glucose-6-phosphate dehydrogenase deficiency (G6PD deficiency).

ALL the corpuscular causes are HEREDITARY except: PNH.

PNH کب وراثی عیلا



II. EXTRA-CORPUSCULAR CAUSES

1. Immune hemolytic anemia:

- Allo-immune: incompatible blood transfusion.
- Auto-immune: autoimmune hemolytic anemia.

2. Infections:

- Malaria, Clostridium welchii.

3. Physical: "Mechanical" = "Trauma to RBCs" [schistocytes]

- March hemoglobinuria. severe intravascular hemolysis following heavy & prolonged exercise in a susceptible individual. * described 1st in soldiers in Army & long distance marathons (March)
- MicroAngiopathic Hemolytic Anemia: DIC, HUS, TTP. rough surface
- Prosthetic cardiac valves.

4. Chemical:

- Drugs: Amphotericin B.
- Toxins: lead, copper, snake venom, RENAL FAILURE.

5. Hypersplenism.

6. Metabolic: Wilson's disease.

Cu metabolism خلل

due to ↓ ceruloplasmin

cut & deposited

- ① Brain → BG (Ectopic)
- ② Liver → cirrhosis
- ③ Kid

- ④ eyes
- ⑤ RBCs

White Knight Love

intra vascular
extra
Physical
G6PD
PNH
Incompatible Bld transf
some types auto immune

also
atypical
Pneumonia
Cold
agglutinin

also
methyl def.
causes hemolytic anemia

Hemolytic uremic syndrome
Thrombotic Thrombocytopenic Purpura
also in I.E.

all physical are intra vascular

Dep: disease of small B-r.
pathology:

endothelial injury
① rough surface
② rough surface
Micro thrombi

platelets Fibrin mesh
RBCs

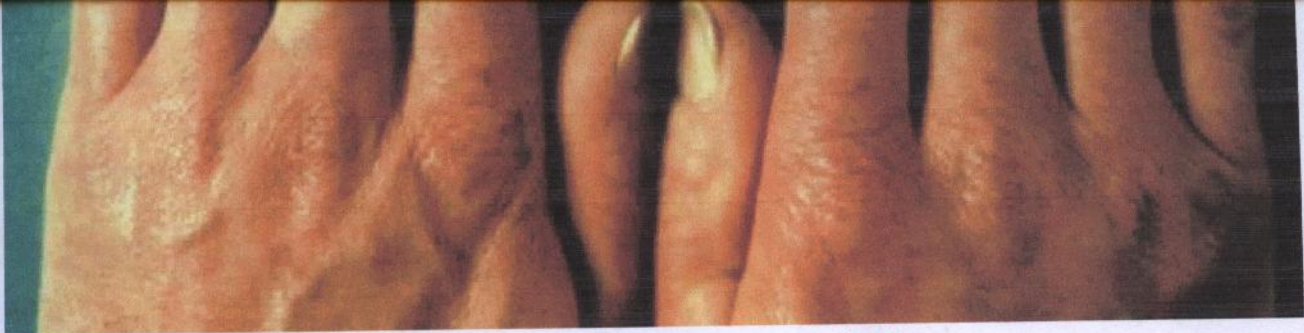
Etiology
• HUS: Toxins (infection) 90% GIT 10% URTI
Rf H.A. E. coli (infective diarrhea: secreting type) (in susceptible children)

• TTP: Abs (not infect) against VWF protease eng → PWF
autoimmune
causes: cong, cancer & pregnancy, susceptible g

① endoth. injury → H.A.
② Microthrombi due to
consume platelets → thrombocytopenia
③ Bleeding tendency due to ↓ platelets in thrombi

↓ toxins excretion

endoth. inj platelet aggregation
activation of factor
↓ platelets in thrombi



TTP

- adult ♀
- auto immune $\left\{ \begin{array}{l} \text{ing} \\ \text{ery} \end{array} \right\} \left\{ \begin{array}{l} \text{cancer} \\ \text{pregnancy} \end{array} \right\}$
- ✓ H.A.
- ✓ Thrombocytopenia
- Neuro: - Common & severe
- stroke & Mentality changes
due to ischemia $\leftarrow \begin{array}{l} \text{endoth. inj} \\ \text{Thromb.} \end{array}$
- Kid: - less common & mild

H.A.
TT
schistocytes

- cortisol
- plasma pheresis

age
etio

CIP

Investigation
لا تفرد بين
CIP والفقره

TT

HUS

children ♂ = ♀ 6M $\rightarrow$ 4y

Infect: Toxins $\left\{ \begin{array}{l} 90\% \text{ GIT (esp E.col)} \\ 10\% \text{ URTI} \end{array} \right\}$

- ✓ H.A.
- ✓ Thrombocytopenia (Platelets $\rightarrow$ $\begin{array}{l} \text{endoth. inj} \\ \text{Sw \& Sd} \end{array}$)
- neuro: - less common, mild
- $\begin{array}{l} \text{Sw \& Sd} \end{array}$

- Kid: - Common & severe
- due to vascular ischemia

(ARF)
H.A.
T.T.
schistocytes

Dialysis

most common cause
of ARF in children
is HUS 10

INVESTIGATIONS

I. Diagnosis of hemolytic anemia:

1. CBC:

RBCs

- Normocytic normochromic anemia: with normal MCV & normal MCHC.
- Macrocytic anemia may occur: in megaloblastic crisis or in severe reticulocytosis.
- Microcytic anemia may occur: in case of thalassemia.
- Reticulocytic count: High, is the rule... Low in aplastic crisis.

Blood film:

may reveal characteristic red cells, e.g. sickle cells.
Physical: schistocytes, Thalassemia: target cell

WBCs & Platelets

- Usually normal:

BUT may ↑ due to hyperactive BM.

2. Bone marrow examination:

- Hyperplastic BM: this is the rule.
- Hypoplastic BM: in aplastic crisis.
- Megaloblastic BM: in megaloblastic crisis.

3. Measure of life span of RBCs:

"using Cr - labelled red cells"

- Shortened life span of RBCs.

4. Bile pigments:

- Serum bilirubin:
- Stools:
- Urine:

increased mainly the indirect.
increased stercobilinogen.
increased urobilinogen, absent bilirubin.

5. Serum LDH:

increased. non specific ↑ AMI Acute P.E.

II. Differentiating Intravascular & Extravascular hemolysis:

- Laboratory features of Intravascular hemolysis:

- Hemoglobinuria.
- Hemosiderinuria.

- Haptoglobin: ↓
- Hemopexin: ↓

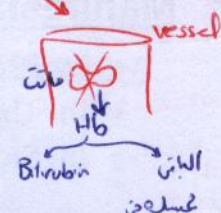
is markedly decreased in plasma.

is markedly decreased in plasma.

III. For diagnosis of the cause:

e.g.

- In PNH: Flow cytometry.
- In Thalassemia: Hemoglobin electrophoresis.
- In Sickle cell anemia: Hemoglobin electrophoresis.



Haptoglobin
Hemopexin
liver

Haptoglobin & Hemopexin
absorptive capacity
Hb urine
Hemosiderinuria
White Knight Love

HEREDITARY SPHEROCYTOSIS

ETIOLOGY

- Hereditary deficiency of a protein in the MEMBRANE of the RBCs leading to:

- RBCs become rigid (less deformable) → destruction especially in the spleen.
- RBCs become more permeable to water → ↑↑ OSMOTIC FRAGILITY.
- RBCs become small & spherical → microspherocytes.

حيث هناك
أما كن خلية
sinusoids
of spleen

CLINICAL PICTURE

1. GENERAL MANIFESTATIONS OF:
2. *Family history*:
3. *Onset*:

HEMOLYTIC ANEMIA. C/P }
is usually positive.
is usually during childhood.

اشبح General anemia
H.A.

INVESTIGATIONS

1. GENERAL INVESTIGATIONS OF:
- ★ 2. Osmotic fragility test: *فيلم*
3. Blood film:

HEMOLYTIC ANEMIA.
↑↑ OSMOTIC FRAGILITY of the RBCs.
microspherocytes.

اشبح H.A.
investigating

TREATMENT

1. Splenectomy: *symptomatic Hb*
2. Transfusion therapy: *< 7 g% Hb severe*

prolongs the life span of the RBCs.
"see before"

Normal RBCs 0.9 g%
0.5 g% (hypotonic) & ruptures of at conc. of fluid
0.5 → 0.3 g%
0.7 → 0.5 g%
بما هذا تفرغ من
الجزء الجداري من بقاء

PAROXYSMAL NOCTURNAL HEMOGLOBINURIA

ETIOLOGY

"UNKNOWN"

من أهم الدروس
ويفضل التعرف على آلية شفي H.A.

- Acquired mutation of BM stem cells → production of cells with abnormal MEMBRANE:

- Absence of certain surface proteins (CD55 & CD59) from cell membrane of all blood cells; this will render the blood cells abnormally affected by the COMPLEMENT SYSTEM:

CD55 CD59

1. RBCs: ↑↑ sensitivity to damage by complement → Hemolytic anemia.
2. Platelets: ↑↑ platelet aggregation by complement → Hypercoagulability & Thrombosis.

oral CD55 & 59 are surface
here, are absent
as not produced
due to mutation
of their producing
stem cell

- Associated BM hypoplasia may lead to:

1. RBCs: Decreased production → aggravation of anemia.
2. Platelets: Decreased production → thrombocytopenia.
3. WBCs: Decreased production → leukopenia.

Pancytopenia

H.A
Thrombosis
Pancytopenia
oral
anemia causes
1- H.A
2- Hypoplastic
3- Fe deficiency
4- Bleeding

Complement up
thrombosis ← RBCs platelets
White Knight Love

CLINICAL PICTURE

- GENERAL: Manifestations of Hemolytic anemia.
- HEMOLYSIS: **INTRAVASCULAR** with Hemoglobinuria (dark urine especially by night).
- PAIN: Attacks of abdominal pain & back pain due to ischemia from microthrombi.
- INFECTION: ↑↑ incidence of infection.
- Complications:
 - Iron deficiency: due to hemosiderinuria & may aggravate the anemia.
 - Aplastic anemia: and Acute myeloid leukemia.
 - Thrombosis: due to mutator (w is the etiology)
 BM hypoplasia
 - PANCYTOPENIA. oral most common sites for thrombosis?
 - 1. Cerebral
 - 2. Mesenteric
 - 3. Liver in hepatic veins "Budd chiri" syndrome - large var.

INVESTIGATIONS

- General investigations of: **Hemolytic anemia.**
- Investigations of: **INTRAVASCULAR HEMOLYSIS.**
- Investigations specific for: **PNH:**
 - Activation of complement in the presence of RBCs → Hemolysis of RBCs, using:
 - Ham test: acidification of serum.
 - Sucrose lysis test: adding sucrose to the serum.
 - Flow cytometry: to demonstrate absent surface proteins on RBCs & WBCs:
 - CD55: DAF (Decay - Accelerating Factor).
 - CD59: Is technique to detect microscopic particles eg: cells & cell pth suspended in stream of fluid & flowing in special optical detection apparatus.

TREATMENT

1. Symptomatic TTI:

- Anemia: **Androgens**, Iron, Transfusion therapy.
- Pain: **Analgesics**.
- Thrombosis: **Anticoagulants**.
- Infection: **Antibiotics**.

2. Corticosteroids: down regulates the complement prednisone 1 mg / Kg / day.

3. BMT. Bone Marrow transplant for format & avoid Malgrancy of mutator

Thrombosis + Bleeding

- TTP
- DIC
- PNH
- SLE
- MPD

CML PRV ETC
wbc n/g
RBC
platelets
General H.A.

RBCs
platelets
WBCs
BM hypoplasia
platelets

Oral
الدم
والدم

Oral
منع
تعد
Oral anticoag.

- PNH
- DIC
- TTP
- SLE
- MPD

HEMOGLOBINOPATHIES

- **Normally:** Hemoglobin is composed of:

- Haem: iron-protoporphyrin complex.
- Globin: protein consisting of 4 polypeptide chains.

- **Normally:** Hemoglobin in the adult is of 3 types:

- Hb A (97 %): its globin is composed of: 2 alpha & 2 Beta polypeptide chains.
- Hb A2 (1-2 %): its globin is composed of: 2 alpha & 2 delta polypeptide chains.
- Hb F (1-2 %): its globin is composed of: 2 alpha & 2 gamma polypeptide chains, and it is the normal Hb in the fetus & diminishes after birth.

- **In Hemoglobinopathies:**

There are abnormalities in the structure of the globin molecule → abnormal types of Hb.

THALASSEMIAS

Hb F

- Hereditary disorders of many types: the most important are alpha & Beta thalassemia.

Alpha Thalassemias:

- There is ↓↓ production of alpha chains leading to production of Hb H (4 Beta) & Hb Bart (4 gamma).
- There is a homozygous form (incompatible with life) & a heterozygous form (slight anemia).

Beta Thalassemias:

- There is ↓↓ production of Beta chains which are replaced by:

gamma chains → production of: Hb F.

Delta chains → production of: Hb A2.

- There are 3 types:

1. **Thalassemia major:** (Homozygous) = Mediterranean anemia

- Hb A is markedly reduced: while Hb F is markedly increased (> 80 – 90 %).
- It presents in adults as: **Mediterranean anemia** or **Cooley's anemia**.

2. **Thalassemia minor:** (Heterozygous) = Thalassemia trait

- Hb A is slightly reduced: with ↑↑ in both Hb F (5-10%) & Hb A2 (5-10 %).
- It presents in adults by: mild microcytic hypochromic anemia, splenomegaly.
- It usually needs no ttt.

3. **Thalassemia intermedia:**

- Hb A is variable: it presents with moderate anemia.

سکڑا
سپلین
سپلین
سپلین
سپلین

ISQ
& clinical

GRF & Thal

iron overload -
Thalassemia?

Thalassemia Major Cooley's anemia Mediterranean anemia

- ① Excessive Hemolysis
- ② Repeated Blood Transfusion
Khatij agut
- ③ ↑ Fe abs. from intestine
(due to upregulation of ferritin
apoferritin system → due to
↑ demand for iron)
نقص Fe اکر
می

CLINICAL PICTURE

1. GENERAL MANIFESTATIONS OF:
2. Family history:
3. Onset:
4. OTHER MANIFESTATIONS:

as
spherocytosis

- Iron overload: e.g. Liver cirrhosis, skin pigmentation, diabetes, CM.
2ry hemochromatosis
- Morphological features: e.g. Mongoloid facies, stunted growth, bone deformities.
due to bone marrow expansion

HEMOLYTIC ANEMIA
is usually positive.
is usually during childhood.

INVESTIGATIONS

1. General investigations of:
2. Investigations of:
3. Investigations specific for:

Hemolytic anemia.
Microcytic hypochromic anemia.

THALASSEMIA:

MCV ↓ < 80 FL
MCHC ↓ < 30 gm/dl

- o Hb electrophoresis: ↑↑ Hb F (> 80 - 90 %): the most important investigation.
normally 1.5% Hb F, 1.5% Hb A2, 97% Hb A.
- o X-ray: Skull (hair-on-end appearance), Long bones (thin cortex & wide medulla).
- o Serum Iron: ↑↑ iron, ↑↑ ferritin, ↑↑ transferrin iron saturation, ↓↓ TIBC.
- o Blood film: characteristic Target cells.

نقص Hb
Hbopathies

DD of other causes of extra vascular hemolytic A.

TREATMENT

1. Specific ttt:

- a. Repeated packed red cell transfusion: to keep Hb > 10 gm %.
- b. Iron chelation: desferrioxamine by SC infusion.
1 mg / day.
- c. Folic acid: not give B12 as large stores
"stem cell Transplantation"
- d. Splenectomy: in case of hypersplenism.

to avoid
Megaloerythrocytosis

Oral
Chelating of copper?
"Penicillamine"

2. New lines of ttt:

BMT, Gene therapy, Hydroxyurea.

3. Prevention:

Prenatal diagnosis
1st trimester: chorionic villi sample → DNA mapping → gene
2nd trimester: amniotic cord blood sample

تشخیص المرض قبل الولادة

Hb A ← انت تفرش قبله
↑ Hb F
White Knight Love
CML
PRV

SICKLE CELL ANEMIA

ETIOLOGY

- A hereditary disorder in which there is production of an abnormal hemoglobin: **Hb S**.
- It may be **homozygous** (sickle cell anemia), or **heterozygous** (sickle cell trait).
- On exposure to **HYPOXIA**, **Infection**, or **Acidosis**, Hb S will form insoluble aggregates:
 - RBCs become sickle-shaped → appear on blood film.
 - RBCs become less deformable → destruction (**Hemolysis**).
 - RBCs show impaired flow → vascular **Occlusion** & tissue infarction.

valine instead of Glutamic acid in a.a. chain of Globin
Hb = Heme + globin
Hypoxia, acidosis, infection
sickle cell anemia

CLINICAL PICTURE

- Incidence: it is common in **black persons** of African origin.

1. HEMOLYTIC ANEMIA. but small spleen "auto splenectomy"

2. VASO-OCCLUSIVE CRISES: occlusion of B.V. due to sickling

- **Bone** infarction: "The most common occlusion"
 - Painful crisis: attacks of severe pain in the **back**, **chest**, or **extremities** ± low grade fever.
 - Avascular necrosis: of the head of the femur.
- Cerebral occlusion: hemiplegia "stroke" & convulsions/fits.
- Pulmonary occlusion: acute pulmonary infarction, or cor pulmonale.
- Hepatic occlusion: abnormal biochemistry & pain. "due to infarction → irritates Capsule"
- **SPLENIC** infarction: autosplenectomy & hyposplenism.
- Renal infarction: hematuria & renal failure.
- Retinal infarction: retinal detachment & blindness.
- Penile occlusion: priapism (persistent & sustained painful erection due to vascular occlusion of vein) & impotence. Blood stagnated in corpora cavernosa.

Priapism or impotence or priapism followed by impotence

3. OTHER CLINICAL MANIFESTATIONS:

- Increased susceptibility to **INFECTIONS**: "Due to hyposplenism" = autosplenectomy = Reticuloendothelial hypoplasia
 - Pneumococcal infections.
 - Osteomyelitis caused by: **Staph. aureus** & **Salmonella**.
 - Delayed growth & development.
 - Gall stones & leg ulcers.] in H.A. but common in SCA

الشعر لونه لاني
Pneumovax
مصل على
الزلة
spleen

INVESTIGATIONS

1. General investigations of:

Hemolytic anemia.

2. Investigations specific for:

SICKLE CELL ANEMIA:

- o Hb electrophoresis: detects the abnormal "Hb S" *the most important investigation.*
- o Blood film: characteristic Sickle cells esp. after inducing hypoxia by adding Na bisulphate.

TREATMENT

1. Specific ttt:

- a. Repeated packed red cell transfusion: to keep Hb > 10 gm %.
- b. Iron chelation: desferrioxamine by SC infusion.
- c. Folic acid: 1 mg / day.
- d. Symptomatic ttt: *Pain of bone*
no splenectomy as there is
auto
splenectomy analgesics for painful crisis.

2. New lines of ttt:

BMT, Gene therapy, Hydroxyurea.

3. Prevention:

Prenatal diagnosis.

G6PD DEFICIENCY

PATHOGENESIS

- Normally:

- RBCs are protected from oxidizing stress by the HMP through producing reduced glutathione.
- RBCs contain G6PD enzyme which is essential for the HMP.

- In G6PD deficiency:

- RBCs do not contain G6PD & therefore will be unable to tolerate oxidizing stress.
- INTRAVASCULAR hemolysis of the RBCs will occur.

مباشرة جوة. حنة

المشكلة تحدث لما يكون السطح موجود

لو طفل عنده G6PD لا ولم يتعرض الى oxid stress لم يمرض

*↓ G6PD
→ oxid. stress*

WhiteKnightLove

DKA in both I & II but mainly in I

1. antidiabetic (I → insulin, II → oral antidiabetic DM)
2. aspirin for life (except if eye abnormality)
- 3.

also
* Duchenne
* Hemophilia

CLINICAL PICTURE

- Incidence: It is an X-linked disease affecting mainly males. (♀ are carriers)
- The patient develops acute intravascular hemolysis when subjected to oxidizing stress:

ACUTE INTRAVASCULAR HEMOLYSIS

- Anemia.
- Hemolytic jaundice.
- Hemoglobinuria.

OXIDIZING STRESSES

DM
1. antidiabetic
2. aspirin
3. antihypertensive
due to early atherosclerosis

- **Iatrogenic:** Aspirin, Antimalarials, Antibacterials (e.g. sulphonamides).
- **Infections:** Pyogenic infections & viral hepatitis.
- **Metabolic:** DKA → free radicals & CRF.
- **Meals:** Ingestion of Fava bean (FAVISM).

drugs infect pain
Oral
- H.A
- oxidizing stress in
G6PD
Abs mediated
RBCs

FAVISM:

- **Incidence:** It is present almost only in Mediterranean populations.
- **Clinical picture:** It presents by acute hemolysis after ingestion of fava beans.
- **Pathogenesis:** It is not well understood, BUT it may be due to abnormal metabolism of beans resulting in production of oxidizing agents.

①
② ↓ G6PD

INVESTIGATIONS

1. General investigations of: Hemolytic anemia.
2. Investigations of: INTRAVASCULAR HEMOLYSIS.
3. Investigations specific for: G6PD deficiency:
 - o Estimation of G6PD.

TREATMENT

1. Avoid oxidative stress: e.g. responsible drugs.
2. Repeated packed red cell transfusion: in severe cases.

Hb % < 7
severe syp
anemic Hf

- PNH in corpuscular
 - Auto imm. in Extra

Intra } vascular
 Extra }

AUTOIMMUNE HEMOLYTIC ANEMIA

A. Due to warm-reacting antibodies: "most active at 37°C"

ETIOLOGY

1. Idiopathic: drug-induced (autoimm.)
 2. Secondary: SLE, CLL, Lymphoma.
 3. Iatrogenic: Drugs (see later).
- Abs sensitizes RBCs (مریض) → diseased
 so, destroyed by spleen
 Extra vascular hemolysis
 young ♀ 20-40y, C/P: fever, skin rash, arthralgia
 GN

CLINICAL PICTURE

1. GENERAL MANIFESTATIONS OF: HEMOLYTIC ANEMIA.
2. SPECIFIC MANIFESTATIONS OF: the cause in secondary cases e.g. SLE.

INVESTIGATIONS

1. General investigations of:
2. Investigations specific for:
3. Investigations for diagnosis of:

Hemolytic anemia.

AIHA: Positive Coomb's test.

the cause in secondary cases e.g. SLE.

TREATMENT

1. CORTICOSTEROIDS:
2. Immunosuppressive drugs: or combined if severe.
3. Transfusion therapy:
4. Splenectomy:

Prednisone 1 mg / Kg / day orally.

e.g. cyclophosphamide.

may be needed in severe cases.

may be needed in severe cases.

also
 ILD
 cyclosporin
 - B.A.
 cyclosporin
 - 7B

B. Due to cold-reacting antibodies:

"most active at 4°C"

I. COLD AGGLUTININ DISEASE

(only Intravascular)

- Presence of antibodies (**IgM**) that cause **Agglutination** of RBCs on exposure to cold.

ETIOLOGY

1. Idiopathic.
2. Secondary:

CLINICAL PICTURE

1. Hemolytic anemia: on exposure to cold.
2. Raynaud's phenomenon: on exposure to cold.

INVESTIGATIONS

1. General investigations of: **Hemolytic anemia.**
2. Investigations specific for: **AIHA:**
3. Investigations for diagnosis of: the cause, e.g. **Mycoplasma pneumonia.**

TREATMENT

1. CORTICOSTEROIDS: of little benefit.
2. Immunosuppressive drugs: e.g. **cyclophosphamide.**
3. Transfusion therapy: may be needed in severe cases.
4. Splenectomy: of little benefit.
5. Avoid exposure to cold.

(+) Cause: **Mycoplasma**: clarythromycin or tetracyclin

II. PAROXYSMAL COLD HEMOGLOBINURIA

- Presence of antibodies (**IgG**) that cause **Hemolysis** of RBCs on exposure to cold.

ETIOLOGY

1. Idiopathic.
2. Secondary: **Syphilis** & **Viral infections.**

CLINICAL PICTURE

- Hemolytic anemia: on exposure to cold.

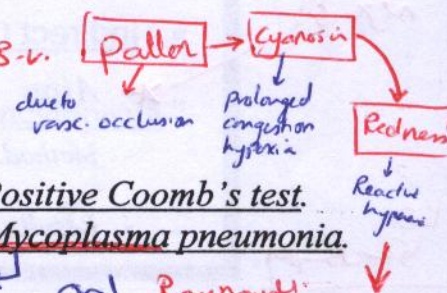
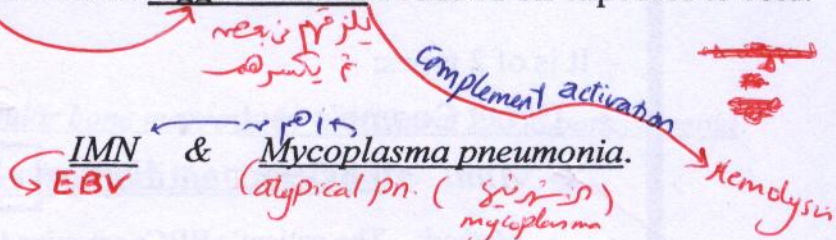
INVESTIGATIONS

1. General investigations of: **Hemolytic anemia.**
2. Investigations specific for: **AIHA:**
3. Investigations for diagnosis of: the cause, e.g. **Syphilis.**

TREATMENT

- Same as: Cold agglutinin disease.

(+) Cause: \$: Penicillin



CXR
Bilat. Fluffy Cotton or GGA

Oral Raynaud's
ing 2ry

- 1 - Exposure to cold
- 2 - Emotional stress
- 3 - Cold agglutinin disease
- 4 - PAD
- 5 - Drug induced "B.B."
6. Collagen vascular disease & vasculitis

RA
SLE
PAN
Scleroderma
& Most common cause Raynaud's is Scleroderma

L Anti \$ Abs

Sulpha

test to detect Abs against RBCs

1. oxid. stress
2. innocent bystander

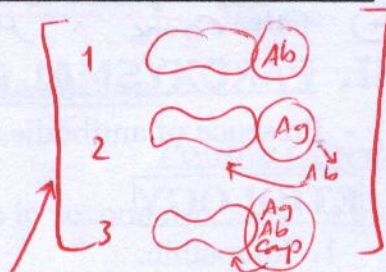
COOMB'S TEST

- It is the test used for diagnosis of autoimmune hemolytic anemia.
- It is of 2 types:
 - Direct Coomb's test: لازقة
 - * Aim: To detect antibodies coating the RBCs.
 - Method: The patient's RBCs are mixed with Coomb's serum.
 - Result: Agglutination indicates a positive direct test.
 - Indirect Coomb's test: حرة
 - * Aim: To detect antibodies circulating freely in the serum.
 - Method: The patient's serum is incubated with compatible RBCs. These RBCs are then washed & mixed with Coomb's serum.
 - Result: Agglutination indicates a positive indirect test.

DRUG INDUCED HEMOLYSIS

- Drugs may induce hemolysis through several mechanisms:

1. Direct damage: of the membrane of the RBCs.
 - e.g. Amphotericin B.
2. Oxidant drugs: in patients with G6PD deficiency.
 - e.g. Antimalarials, Aspirin, Sulphonamide



3. IMMUNE MECHANISMS: (Abs mediated) ازای ایواندایس RBCs بواسطه ۳imm. مکانیسم

- Autoimmune reaction:
 - The drug induces the production of an antibody which destroys the RBCs.
 - e.g. alpha-methyl dopa, anti-HTV → acts as Ag in body induce Abs →
- Hapten-like reaction:
 - The drug binds to the membrane of the RBC acting as a hapten.
 - e.g. penicillin → acts as Incomplete Ag (hapten) →
- Innocent bystander reaction: "Immune complex"
 - The drug binds to its antibody on the surface of the RBC → complement activation.
 - e.g. chlorpropamide & sulphonamides.

استرخ
ethio
warm Abs
CAH & AIHA

وهور
2 الی
(Hapten)
در سطح
RBCs
Ag → Abs →

oral hypoglycemic drug → Ag not reacts to RBCs but releases Ab & both (Ag-Ab complex) → attach to RBC
Immune complex ← Ag+Ab+comp → White Knight Love

كل النيميا ه ادلى لاحرفا مهم
والنوع الصغرة سؤال قصير
وكمان سفوف بعنف

APLASTIC ANEMIA

- SQ
- Oral

DEFINITION

انتاج الخلايا
ضعيف

infects drug

- A disease characterized by: hypocellular bone marrow & peripheral blood pancytopenia.
- Aplastic anemia: anemia due to Bone marrow failure.

القاعدة

نابستثناء نادر
يكونه خط واحد بس! لك
واقف

ETIOLOGY

I. APLASTIC ANEMIA

صوم زي اسمك

"Pancytopenia"

a. Hereditary: Fanconi's anemia.

hereditary
also
Fanconi
syndrome
↓
renal tubular
defect

b. Acquired:

نفس انواعه نفس
Dose Dependent
↓
good prognosis
non D.D.
v. bad prognosis

Mostly autoimmune (although
no Abs detected in Blood) but
due to good response to imm ↓

1. Idiopathic: The most common cause (about 50% of the cases).

2. Iatrogenic: Dose-dependent OR Non Dose-dependent (idiosyncratic)

Reversible
كل شئ يقى
بالتدريج
وله تركت
المواد
يرجع تاني
طبعية
وبالتدريج
توفى

- 1 - Antibiotics: e.g. **CHLORAMPHENICOL**
- 2 - Anti-inflammatory: e.g. NSAIDs & Gold.
- 3 - Antiepileptics: e.g. phenytoin, Hydantoin, Epanutin
- 4 - Antithyroid: e.g. carbimazole.
- 5 - Antidiabetics: e.g. chlorpropamide.
- 6 - Antineoplastics: e.g. chlorambucil.

auto-immune
H.A.
innocent
bystander

oral
Hou EBV
causes
anemia?
1- Aplastic
2- Cold agglutinin

3. Infections: **PARVOVIRUS B19, HBV, HCV, HIV, EBV.**

4. Insecticides: and chemicals as **BENZENE.**

5. Immune: SLE (rare). warm reacting

6. Irradiation.

7. OTHERS: PNH, Pregnancy.

Aplastic Anemia
& Leukemia

also
aplastic
crisis

Head chry pericarditis
E.P.
Long chry pleurisy
non-infective
Pneumonia

B.m. CSS & ES ↓
associated hypoplasia
if toxic inhibition of B.m. (toxemia of pregnancy)

II. UNICELLULAR APLASTIA

v. rare

"Monocytopenia"

خط واحد
بس الى عطل

a. Pure red cell aplasia: e.g. associated with Thymoma, aplastic crisis of HA.

b. Granulocytopenia: e.g. Cyclic neutropenia.

part of imm. system
Produces lymphocytes → T lymphocytes
immune system

c. Thrombocytopenia: e.g. TAR syndrome (Thrombocytopenia, Absent Radius, ASD).

تاني وتروع
فلية بعد حاجه شتر ترجع طبيعية وكنا
on & off

If - oma
↓
defect in imm. system
White Knight Love
Abs against lymphocytes

CLINICAL PICTURE



- **ANEMIA** (due to ↓ RBCs).
- **INFECTIONS** (due to ↓ WBCs).
- **BLEEDING** (due to ↓ Platelets).

PANCYTOPENIA

Mouth & throat infections

شرح → General C/P of anemia

شرح
درسی
hemostasis

Criteria of Bleeding
due to ↓ platelets

INVESTIGATIONS

1. CBC:

"Pancytopenia"

- RBCs: NN anemia: with reticulocytopenia.
- WBCs: Leukopenia. <4000 اکب
- PLATELETS: Thrombocytopenia. <150,000 اکب

↓ RBCs ↓ Hematocrit
↓ Hb% ↓ HbC
↓ HCV ↓ HbC

Persistently ↓
< 0.5%

ب.ا.
N N reticulocytosis

2. Bone marrow examination:

"Aspiration & biopsy"

- Hypocellular fatty BM devoid of hematopoietic precursor cells.

= acellular
Fat cells only ← cells of B.M.

غير موجود

3. Investigations for the cause:

e.g. markers for HBV & HCV.

Causes of death

Bleeding
infection

HBV surface Ag
HBs Ag

Ab_s against
HCV

DIFFERENTIAL DIAGNOSIS

1. Other causes of: PANCYTOPENIA. eg SLE: ...
2. Acute leukemia. (fever, infection, anemia, Bleeding tendency)

TREATMENT

I. Supportive TTT:

- Withdrawal of the offending drug & ttt of the cause, **plus:**

1. For anemia: packed RBCs transfusion.
2. For infections: antibiotics, G-CSF.
3. For bleeding: platelet transfusion.

eg Hepatitis

if Hb% < 7%
severe sy.p.
anemic H.f.

recombinant (by DNA technology)

Granulocyte Colony Stimulating Factor
بزرگ شدن گرانولوسیت ها
مفید در عفونتهای باکتریایی

II. Specific TTT:

لا علاج الوحد
للعيان

طالوت شريب

1. BMT:

It is the only curative ttt & is indicated in

- **Progressive:** severe aplastic anemia.
- **Patients less than:** 45 years.
- **Presence of:** a suitable donor.

above 45 → جربو → graft rejection

For Idiopathic & Idiosyncrasy
50%

2. Immunosuppressive therapy:

"Undefined mechanisms"

- Cyclosporin.
- Corticosteroids: High dose.
- Antithymocyte globulin (ATG) → T lymphocyte
= Anti lymphocyte → ALG

20mg/kg/day

Most efficient

3. Bone marrow stimulants:

- Androgens.

- Infusion of animal derived Abs against human thymocytes with a good response in patients with idiopathic Aplastic Anemia

(auto immune)

Oral

also ATG is used for imm. to avoid rejection in BM transplant

* Cyclosporin

- 1 * B.A.
- 2 * Aplastic anemia
- 3 * BM transplant to avoid rejection
- 4 * Behcet's

Enumerate the causes,

CAUSES OF PANCYTOPENIA

- Bone marrow failure: Aplastic anemia.
- Bone marrow infiltration. Myelophthisic anemia.
Myelopathic
- Megaloblastic anemia. → ↓ F.A or ↓ B₁₂ or ↓ Both
- Myelodysplastic syndromes. → Def: failure of maturation (not proliferation) of stem cells of one or two or three cell lines
Leading to mono or Bi or Pancytopenia
- PNH. → Pancytopenia Thrombosis H.A.
- SLE. → Def: failure of maturation (not proliferation) of stem cells of one or two or three cell lines
Leading to mono or Bi or Pancytopenia
- Overwhelming infections.
- Disseminated TB. Typical Tuberculous granuloma
- Hypersplenism. → breaks cells may be mono or Bi or pancytopenia

• Eto → Idiopathic (most common)
2ry → Radiotherapy
Chemo therapy
• May be associated i Sideroblastic anemia

CAUSES OF BM INFILTRATION

"BM biopsy is the diagnostic procedure"

- Myelofibrosis: B.M. → replaced by fibrous tissue
 - Idiopathic.
- Malignancy:
 - Blood malignancies: Leukemias, Lymphomas.
 - Solid malignancies: BM metastases.
- Metabolic:
 - Lipid storage diseases: Gaucher's disease.
- Massive infections:
 - TB (miliary). Typical tuberculous granuloma
 - Fungi.

CHLORAMPHENICOL & BM SUPPRESSION

- Dose-related suppression:
 - Transient reversible aplastic anemia.
- Non Dose-related suppression: "Idiosyncrasy"
 - Severe fatal irreversible aplastic anemia.

MEGALOBLASTIC ANEMIA

DEFINITION

- Anemia in which there is impaired DNA synthesis due to deficiency of Vitamin B12 or / and folic acid:

- Delayed division of the rapidly proliferating cells (Hematopoietic cells, GIT, Skin).
- Production of MEGALOBLASTS in the BM & MACROCYTES in the peripheral blood.

ETIOLOGY

I. VITAMIN B12 DEFICIENCY

1. Decreased intake:

- Lack of animal products. (poverty)
- Vegetarian individuals.

2. Decreased absorption:

- Deficient intrinsic factor: B_{12} & F.A.
- General Malabsorption syndrome: B_{12} only
- Specific Vitamin B12 malabsorption: B_{12} only

3. Increased demand:

- Resection
 - Crohn's disease
 - intestinal T.B
- Infancy.
 - Pregnancy. ↑ cells turnover
 - Malignancy. ↑ cells turnover
 - Chronic hemolysis. RBCs → Hb → B.M. → ↑ demand

pernicious anemia, gastrectomy, atrophic gastritis.

general causes of malabsorption including bacterial overgrowth.

Diphyllobothrium latum infestation or ileal affection.

- B12 only for nervous system
CNS & P.N.
for myelin sheath & ↑ conduction

* normally Bacteria in large int. while S.I. no Bact

* ent : ↓ int. motility → stagnation of int. contents
Fermentation

* Result: Bacteria cause int. contents → nonabsorbable

* H : Antibiotics

II. FOLIC ACID DEFICIENCY

1. Decreased intake:

- Lack of vegetables.
 - Excessive alcohol intake.
- severe anorexia
 - ↓ abs. f.A.
 - ↓ metabolism f.A.

2. Decreased absorption:

- General Malabsorption syndrome: general causes of malabsorption.
- Specific folic acid malabsorption: **Drugs:** anticonvulsants, CCPs.

Anticonvulsants CCPs → ↓ abs. f.A. → ↓ f.A. → ↓ DNA synthesis → Oral

antagonist Action

3. Increased demand:

- Infancy.
- Pregnancy.
- Malignancy.
- Chronic hemolysis.

4. Folic acid antagonists:

- ① Methotrexate.
- ② Co-trimoxazole.

③ 6-Mercaptopurine (6 MP)

anti bact. (Pneumocystis carinii)

anti cancer

Abs in Blood
ass. with autoimmune
Response to Immuno
suppress

PERNICIOUS ANEMIA

Atrophy of the gastric mucosa → decreased secretion of intrinsic factor (IF) & B12 deficiency.

It is probably due to: autoimmune disease which may be genetically determined leading to:

- Antiparietal cell antibodies that block the production of IF.
- Anti-IF antibodies that block the function of IF.

It may be associated with other autoimmune diseases:

- 1 - Autoimmune thyroiditis. - hypothyroidism
- 2 - Addison's disease. - 1st common cause autoimmune
- 3 - Vitiligo. - " " TB

gene
auto immune
gene auto Type I DM
mechanism of autoimm. disease
virus
anti islet cells
anti insulin Ab

④ complication stomach cancer - hypopigmentation

PATHOPHYSIOLOGY

بلد ما ينقسم فالعدد ينزول
الخلايا كبيرة العديلة
الأنسجة يصغر

Vitamin B12 & folic acid deficiency: Both are essential for DNA synthesis, so their deficiency will lead to deficient DNA synthesis in the dividing cells → **Delayed division.**

In the Bone Marrow: Delayed division will result in the production of MEGALOBLASTS instead of the Normoblasts. Since these Megaloblasts are abnormal cells, they will be destroyed in the bone marrow by macrophages (**Intramedullary hemolysis**).

In the peripheral blood: Megaloblasts that are formed in the bone marrow will lose their nuclei and reach the peripheral blood as MACROCYTES which are large cells with increased MCV. Many of these Macrocytes are taken by the spleen and destroyed (**Extramedullary hemolysis**).

ANEMIA will result due to:

- Delayed division of erythroid precursors.
- Excessive hemolysis (Intramedullary & Extramedullary).

LEUKOPENIA & THROMBOCYTOPENIA: similarly occur due to deficient DNA synthesis.

PANCYTOPENIA: will finally occur.

OTHERS:

GIT: Cells in the GIT show the same defect, leading to secondary atrophy of the epithelial cells of the: **tongue, stomach, small intestine.**

CNS: Inability to synthesize myelin is present **ONLY** in B12 deficiency and leads to neurological manifestations (Absent in folic acid deficiency).

if B12

CLINICAL PICTURE

1. HEMATOLOGICAL MANIFESTATIONS

- **ANEMIA** (due to ↓ RBCs).
- **INFECTIONS** (due to ↓ WBCs).
- **BLEEDING** (due to ↓ Platelets).

PANCYTOPENIA (انسحاب)

- **HEPATOSPLENOMEGALY.** *due to extra medullary hemolysis*

2. GIT MANIFESTATIONS

- Tongue: **Atrophic glossitis** (red glazed tongue). *also fe def anemia*
- Stomach: **Atrophic gastritis** (dyspepsia, anorexia, nausea, vomiting).
- Intestine: **Intestinal Atrophy** (abdominal pain, diarrhoea, malabsorption).

3. NEUROLOGICAL MANIFESTATIONS

- Peripheral neuropathy. *mainly sensory*
- SCD of the spinal cord (refer to neurology). *Sub acute combined degeneration*

tracts demyelinated *Pyramidal tract* *post column*

malabsorption
atrophy (↓ B12 & fol c)
more malabs.
"Only In B12 Deficiency"
سجی، ۱۲

4. ASSOCIATED AUTOIMMUNE DISEASES

- Autoimmune thyroiditis. → *کمر طرا*
- Addison's disease. → *کمر طرا*

"Only In Pernicious anemia"
سجی، ۱۲

INVESTIGATIONS

1. CBC:

a) RBCs:

• Features of macrocytic anemia:

- Decreased: Red cell count, Hemoglobin level, Hematocrit value.
- Increased: MCV (**LARGE RBCs**).

- Reticulocytosis: after giving ttt (anemia under ttt).

B.m hyperactive

b) WBCs:

- Leukopenia: →
- **LARGE NEUTROPHILS**

with shift to the **right**.
(Hypersegmented).

not band

البند
الوحيد
أو
(Band) ← left
Bacteria

c) Platelets:

- Thrombocytopenia.
- **LARGE PLATELETS**.

2. Bone marrow examination:

- Hypercellular **megaloblastic** bone marrow.
- Giant cells with abnormal morphology.

Also in
Megaloblastic
crisis
of H.A.

3. Blood chemistry:

- Increased: ^{mild} serum indirect bilirubin. (hemolysis)
- Increased: serum iron. — hemolysis
- Increased: serum LDH. — ineffective erythropoiesis (↓ consumption)

لا يظهر
clinically
لأنه
من أعلى
2.5~

4. Serum B12 & serum folic acid:

- Decreased.

“done by radio-immunoassay”
radioisotope باستخدام

5. Schilling test:

“Only In B12 Deficiency” [measures B12 ↓ absorption only]

- Unlabelled B12 is given: Parental (1000 ug IV) to saturate the body stores. إلى المخازن
- Radiolabelled B12 is then given: Oral (1 ug orally). فاعلية هضمه لا تتغير
- The patient's urine is collected for 48 hours: measure excreted Radiolabelled B12.

- If excretion is low:

- In **pernicious anemia**: excretion becomes normal after giving IF orally.
- In **bacterial overgrowth**: excretion becomes normal after giving Antibiotics.
- In **pancreatic insufficiency**: excretion becomes normal after giving Pancreatic enzymes.

B12 malabsorption is diagnosed:

Differential
Schilling
Quantitative
Schilling

لا يظهر
لأنه هودنه
التي هاضمة
100ug
لا يذهب أبداً
التي stores
لأنه فاعلة

فان حاجب حمض
B12
فان في البول
الطفر في البول

لو قليله
في البول
مقارنة ببق
abs.
في البول

على
التي
absorption
Kid. fx test
excretion

WhiteKnightLove

6. Serology:“ Only In Pernicious anemia ”

- Antiparietal cell antibodies.
- Anti-IF antibodies.

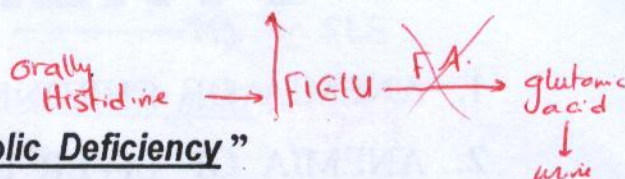
7. FIGLU test:“ Only In Folic Deficiency ”- Normally:

Form imino Glutamic acid

Orally given HISTIDINE is transformed into FIGLU which is converted in the presence of folic acid into glutamic acid which is excreted in urine.

- In folic acid deficiency:

Oral administration of HISTIDINE will lead to excessive excretion of FIGLU in urine (instead of glutamic acid).

8. Therapeutic tests:

- Giving small doses of Vitamin B12 or Folic acid → Reticulocytosis.

Hyponactive B.M.

TREATMENT1. Replacement therapy:a) In B12 deficiency:

(Parenteral)

- Hydroxycobalamin or cyanocobalamin: 500 – 1000 μ g IM / day for 2 weeks.
- Then: once / week until anemia is corrected.
- Then: once / month for life. esp. pernicious anemia

b) In folic acid deficiency:

(Oral) or (parenteral)

- Folic acid: 1-5 mg / day orally.
- Parenteral administration may be needed: e.g. in malabsorption.
- Therapy for: 1 month is sufficient to correct the anemia.
- B12 deficiency should be excluded before giving folic acid since it may aggravate: the neurological manifestations.

Oral

2. Transfusion therapy:

- Packed red cell transfusion may be needed in cases of severe anemia:

- Hemoglobin: < 7 gm %.
- Marked symptoms of anemia.
- Anemic HF.

IF B12 هو اللى ناقص (neuro manifest) → واعطاه F.A. → فسيكون neurological manifestations

(دواء اللى يعطى فيه B12 وضاع) permanent (لا رجعة كثيره وتبقى عاقله)

bm hyperactive ← F.A.

B12 يعطى

اللى already

تبقى

فيعمل اكثر

3. TTT of the cause & symptomatic ttt of anemia.

Leg: Antibiotics (Bact. overgrowth)
Leg: diuretics (H.f.)

White Knight Lane

OTHER ANEMIAS

1. ANEMIA OF CHRONIC DISEASE (ACD).
2. ANEMIA OF LIVER DISEASE.
3. ANEMIA OF UREMIA.
4. SIDEROBLASTIC ANEMIA.
5. ANEMIA OF ENDOCRINE DISORDERS.
6. ANEMIA OF PREGNANCY.
7. ACUTE POST-HEMORRHAGIC ANEMIA.

من مسوح انك تلتزم فير في السفوي

ANEMIA OF CHRONIC DISEASE (ACD)

DEFINITION

- It is a type of anemia seen in chronic illness.
- Incidence: it is the 2nd most common type of anemia.
- Severity: it is usually mild to moderate.

after Fe def. anemia

as chronic → time for compensatory mechanisms

ETIOLOGY

- tissue inflammation [1. Chronic infection (e.g. TB). *Bronchectasis*
- 2. Chronic inflammation (e.g. RA, SLE, IBD). *infection*
- tissue damage (injury) [3. Malignancy (Blood, Solid). *infl. Bowel disease*

PATHOGENESIS

- 1. Reduced life span of RBCs. *أقل عمر*
 - 2. Impaired release of iron from stores in organs. *فول*
 - 3. Erythropoietin (EPO) defect: → ↓ RBCs
 - ↓ production of EPO.
 - ↓ response to EPO in the BM. renders BM non responsive to EPO
- infection & inflammation & injury → Cytokines IL1 → affinity of macrophages for iron → BM, liver, spleen in macrophages
- used for turnover of cells due to tissue inflammation → *لوحلت BM تلاقا الحديد كثر فيه*

CLINICAL PICTURE

1. Clinical picture of the cause. → TB or SLE
2. General clinical picture of anemia (*usually mild*). اشح

INVESTIGATIONS

1. Investigations of the cause.
2. Microcytic hypochromic anemia or: NN anemia.
3. Serum iron: decreased, Serum ferritin: normal or increased.

DIFFERENTIAL DIAGNOSIS

- Causes of: Microcytic anemia:

1. Iron deficiency anemia.
2. *Thalassemia*.
3. *Sideroblastic anemia*.
4. *Anemia of chronic disease* (ACD).

	iron	ferritin الحديد المخزن
Fe def	↓	↓
Thalassemia	↑	↑
Sideroblastic	↑	↑
ACD	↓	↑

كلما
عقل واحد
اشح
Scheme

TREATMENT

1. TTT of the cause. eg. SLE → cortisol
Anti-TB
2. Recombinant EPO. if ↓ EPO is the cause

من زى الخلل لـ serum iron زى فى الـ التهاب
هنا ACD خالفت ferritin (الخازنة) Peripher Bld
لا يتبع الـ serum Fe
نرى زى زى ferritin pln
(Inflammatory marker) Acute phase Reactant
يزيد مع الـ التهاب
tissue damage
لحرق، انخرع الـ المرض
Acute or Chronic

ANEMIA OF LIVER DISEASE

1. Liver cell failure: Normo Micro Macro Refer to "Liver notes".
2. Hepatitis: Aplastic anemia with HBV, HCV.
3. Wilson's disease: (Cu) Hemolytic anemia.
4. HCC: ACD.
5. Lipid storage disease: Gaucher Myelophthisic anemia (BM infiltration).

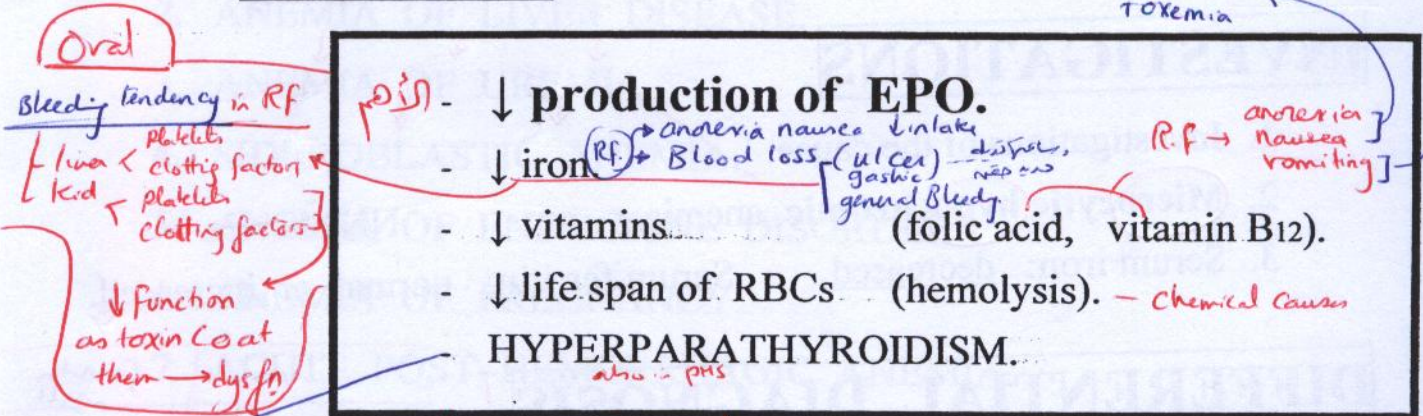
Most common cause of Chronic R.F. in adult → DM & in Egypt 1. DM
 Most Common " " Acute R.F. in children → HUS 2. Chronic pyelo-nephritis

39

ANEMIA OF UREMIA

- Incidence: Common.
- Severity: Usually related to the degree of uremia.

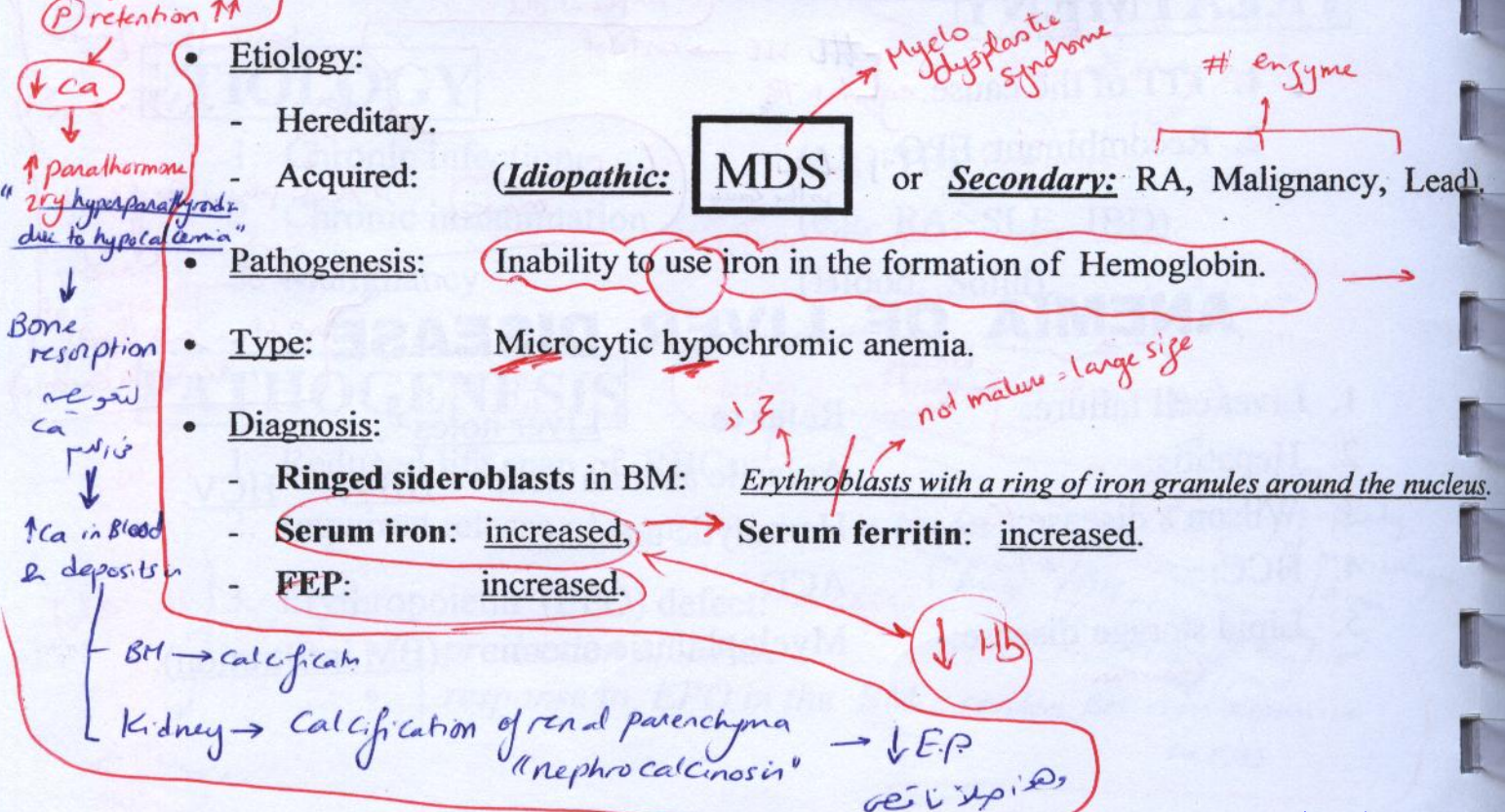
• PATHOGENESIS:



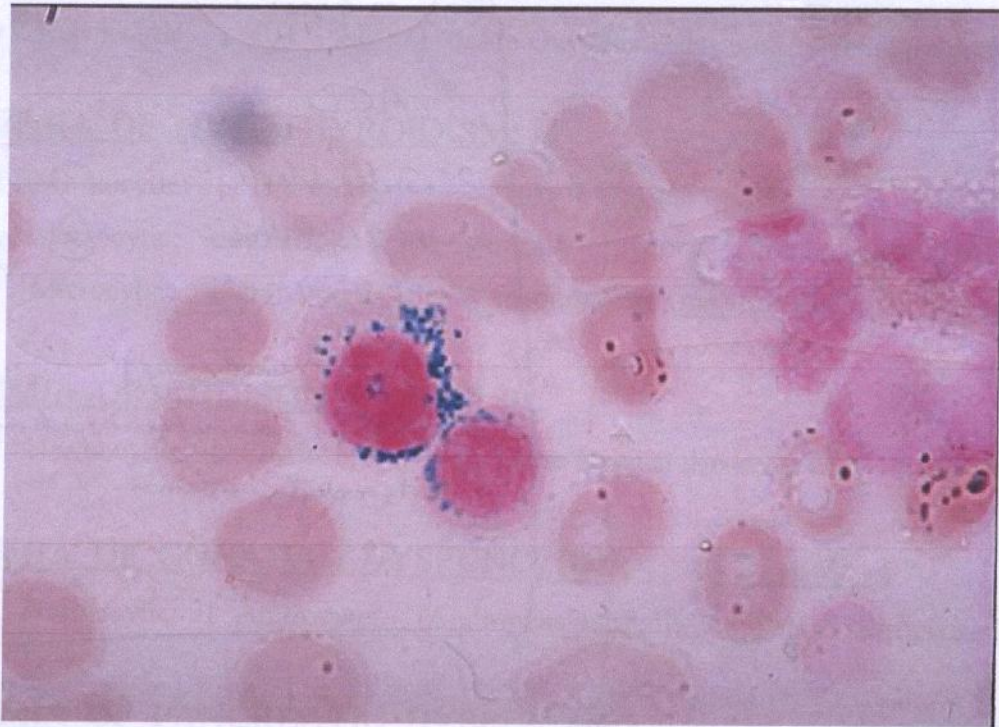
- CP: CP of uremia + general CP of anemia.
 - Investigations: NN anemia + SCHISTOCYTES + impaired renal functions.
 - Treatment: TTT of uremia, recombinant EPO.
- Oral
- Kidney endocrine
- Renin
 - Erythropoietin
 - Vit D metabolites
- Kidney function failure
- ↓ excretion (P)
- (P) retention ↑
- ↓ Ca
- ↑ parathormone
- "2ry hyperparathyroidism due to hypocalcemia"
- Bone resorption
- ↑ Ca in blood
- 2 deposits
- BM → calcification
- Kidney → Calcification of renal parenchyma "nephrocalcinosis" → ↓ E.P

SIDEROBLASTIC ANEMIA

- Etiology:
 - Hereditary.
 - Acquired: (Idiopathic: **MDS** or Secondary: RA, Malignancy, Lead).
- Pathogenesis: Inability to use iron in the formation of Hemoglobin.
- Type: Microcytic hypochromic anemia.
- Diagnosis:
 - Ringed sideroblasts in BM: Erythroblasts with a ring of iron granules around the nucleus.
 - Serum iron: increased, Serum ferritin: increased.
 - FEP: increased.



Ringed sideroblasts



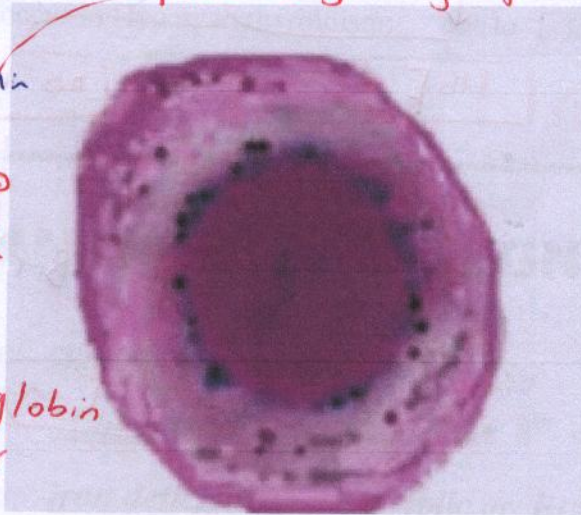
↑ Fe + ↑ protoporphyrin

↓ enzyme X

Heme → + globin

↓ Hb

Free Erythrocyte protoporphyrin



- Blast
- large
- nucleus
- Sidero = Fe granules around nucleus

لا يتم إنتاج هيموجلوبين

oral 

How Cancer → anemia

Scheme of DD. of Micro Hypo anemia

Cancer in general

Cancer (specific)

Stomach 8 causes

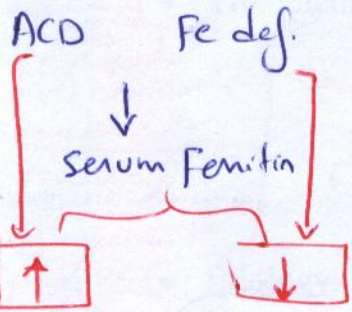
1. ACD
2. Sideroblastic
3. Myelophthisic
4. Aplastic (due to chemotherapy)
5. PMS (paraneoplastic syndrome)
6. Hemolytic anemia

- ① Fe def. anemia
- ② Megaloblastic (↓ intrinsic factor)

⊕ 6

in physical causes
TTP (↓ ^{ing} 2ry ← cancering preg)

[Serum Fe]



الو
لا
م
Fe
Serum ferritin

Thalassemia

Sideroblastic

↓ ^{steroids}
Serum ferritin

Hb electrophoresis

[Hb F]

[no Hb F]

↓ ^{سلي}
BM biopsy

[Ring sideroblasts]

ANEMIA OF ENDOCRINE DISORDERS

1. ANEMIA OF HYPOPITUITARISM:

- Normocytic: ↓ GH → ↓ tissue Oxygen needs → ↓ renal production of EPO.

2. ANEMIA OF HYPOTHYROIDISM:

- Normocytic: ↓ Thyroxine → ↓ tissue Oxygen needs → ↓ renal production of EPO.
- Macrocytic: due to folic or B12 deficiency (1) or due to associated pernicious anemia. (2) ↑ cholesterol w/ deposits in cell membrane → large cells
- Microcytic: due to iron deficiency secondary to malabsorption (1) & menorrhagia in females. (2)

بالرأس
ميتنقص
أكثر

3. ANEMIA OF ADDISON'S DISEASE:

- Normocytic: ↓ Cortisol → ↓ tissue Oxygen needs → ↓ renal production of EPO.

دوره
علائق
از بدن
فتقر
NN

4. ANEMIA OF GONADAL DYSFUNCTION: [In males]

- Normocytic: ↓ Androgens (Androgens normally stimulate erythropoiesis in BM).

عكس
Cushing
بالرأسه أخطر

5. ANEMIA OF PANCREATIC DYSFUNCTION:

- Anemia is common in DM: due to chronic complications of DM, e.g. CRF.

Chronic
infection

6. ANEMIA OF PARATHYROID DYSFUNCTION:

- Anemia may occur in Hyperparathyroidism: due to ↓ EPO production & BM calcification.

(nephrocalcinosis)

نسبة

ANEMIA OF PREGNANCY

oral

- Incidence: common.
- Severity: Mild to moderate, (about the 8th week of pregnancy).
- Etiology: iron deficiency, folic or B12 deficiency.

(3) dilutional anemia

(1) ↑ demand

(2) Toxemia
of pregnancy

hyperolemia.

بعد الأسبوع ٢٠
و ده نادر

SQ
Oral 1000 emergency
Acute severe Bleed

ACUTE POST-HEMORRHAGIC ANEMIA

ETIOLOGY

"Acute severe bleeding"

1. Trauma.
2. Surgery.
3. GIT ulcers.
4. Hemorrhagic blood diseases: e.g. Hemophilia, Purpura.

CLINICAL PICTURE

1. Evidence of: BLEEDING.

(Bleeding from multiple sites suggests: Hemorrhagic blood diseases).

2. General clinical picture of anemia, manifestations depend on:

- **Rate** of bleeding. "no time for compensation"
- **Amount** of bleeding.
- **Time** between bleeding & presentaion.

3. There are 2 chronological CLINICAL STAGES:

- A) FIRST STAGE: (lasts 1 – 3 days)

- Manifestations of hypovolemia.

- B) SECOND STAGE: (after 1 – 3 days)

- Manifestations of hypovolemia disappear.

- Manifestations of anemia.

Signs of dehydration
eg: sunken eyes,
dry eye, tongue, mouth
loss of skin turgor

hypotension → may reach shock
rapid weak pulse
cold extremities
Oliguria → may reach ARF

شرح

التفسير

① RBF ↓ → ↑ renin → Aldosterone → Na & H₂O retention
② ↓ plasma → ↑ NA relatively → osmoreceptors → ADH → H₂O retention
→ hypoth. → pit

العيان فقر
plasma
كثير فاصحي
RBCs
فان مركزة

في البلازما
قليلة
anemia
is masked
due to
concentration
effect

RBCs ال
masked
فان رجع حجم البلازما طبيعي

INVESTIGATIONS

1. Investigations of the cause.

2. CBC:

- RBCs: anemia (normocytic or macrocytic), reticulocytosis.
- WBCs: leukocytosis.
- PLATELETS: thrombocytosis (reactive).

Bm
hyperactive

dry
not very or essential

hge causes
↑ Retics.

Bm hyper
White Knight Love

GIT: endoscopy
hgc: bleeding profile

TREATMENT

1. Treatment of the cause. [eg: GIT : chemotherapy]
2. Symptomatic treatment: [eg: hgic : Bleeding prophylaxis]

- e.g.**
- Correction of hypovolemia, e.g. ^{whole} Blood transfusion.
 - For anemia. multivitamin (not packed RBCs)

f.f.A. only
not need B₁₂ as stores not easily depleted

LEUKEMIAS

نسرطان الدم الأبيض WBC

DEFINITION

- Neoplasms that arise from malignant transformation of hematopoietic or lymphoid cells.
- Leukemic cells (abnormal Leukocytes) proliferate primarily in the BM, & then circulate in the peripheral blood and infiltrate other tissues.

انضغ المورقة
المخاطية

RRK1 - PRU
platelets essential

①

of B.m. cells

②

Liver
spleen
LNS
Thymus
B.m.

ETIOLOGY

- The cause is UNKNOWN.
- Predisposing factors include:
 - Genetic: Incidence in identical twins & in chromosomal disorders, e.g. Down's syndrome.
 - Environmental: Irradiation, Chemicals as Benzene.
 - Viral infection: Retroviruses.
 - Pre-existing disorders: PNH, MDS. Failure of maturation

أخوة كانه فيجول

لغوية اختلصوا في النكل والتصرفات هناك تبارا
lyphoid tissue ~ lymphoma

also
in
Aplastic
anemia

one of its
complication is Acute leukemia

name

oral

HTLV

Human T-lymphotropic virus

① ✓
② ✓
③ X

HIV

مألووش دعوة بالوكيميا

CLASSIFICATION

1. According to the clinical course:

- Acute leukemia: characterized by proliferation of IMMATURE CELLS = **BLASTS**.
- Chronic leukemia: characterized by proliferation of MATURE CELLS = **CYTES**.

انضغ الصفة
المخاطية

2. According to the cell type:

- Lymphatic leukemia. From Lymphocytes
- Myeloid leukemia. From Neutrophils, eosinophils, Basophils, Monocytes

mostly of sm & may be of liver spleen LNS

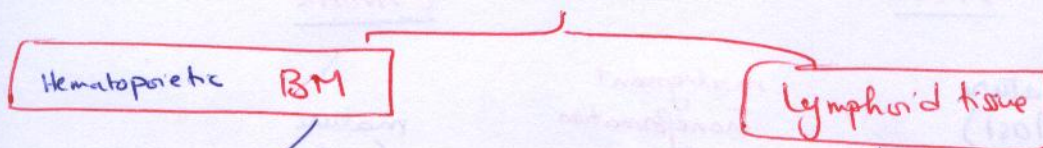
granulocytes

more from granulocytes
more from neutrophils

INCIDENCE

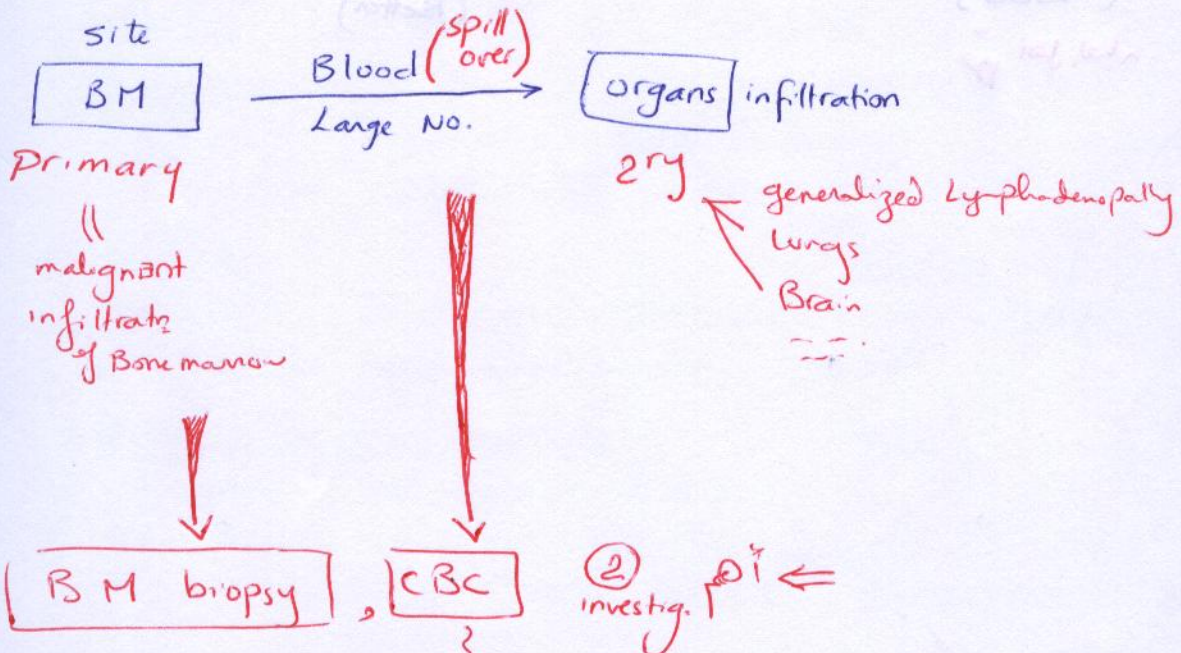
- Acute & chronic leukemia are nearly of equal incidence.
- Age: leukemia may affect any age, HOWEVER:
 - ALL: more common in children & young adults.
 - AML: more common in adults.
 - CLL: more common in old age.
 - CML: more common in middle & old age.

Leukemia

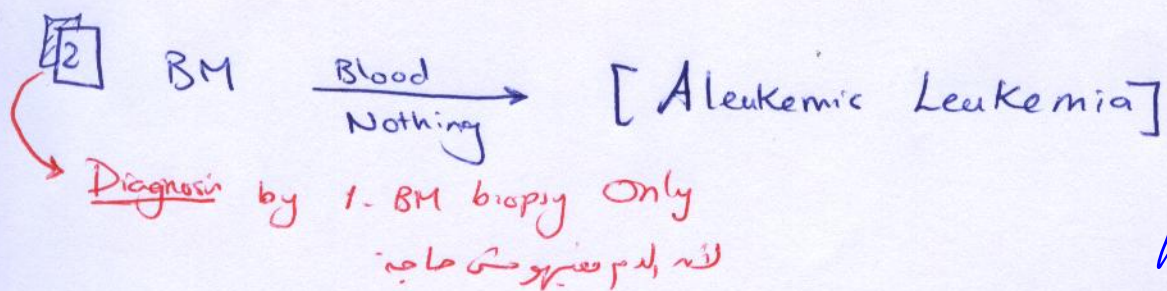
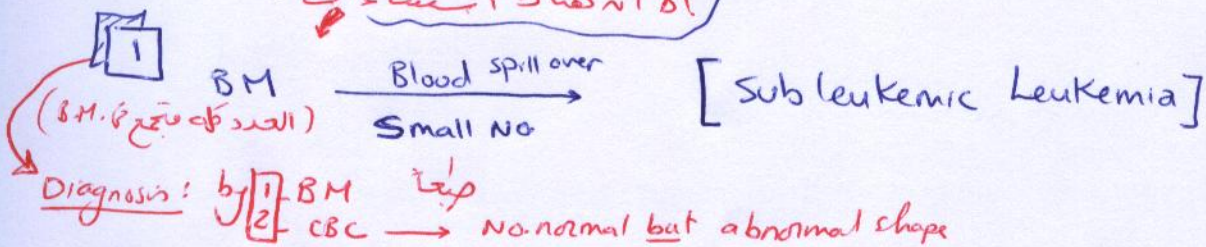


- RBCs → erythroid
- platelets → Megakaryocytic } *v. rare*
- WBCs
 - neutrophils
 - Monocytes
 - eosinophils
 - Basophils
 - Lymphocytes

Liver
spleen
LNs
Thymus
B.m



مقدار WBCs
التي المفروضة لا تزيد عن ١١ ألف يوميل ملون
ومكانه في الدم غريب
إلا أنه هناك استثناءات



Acute

Immature
(Blast)

malignant
transformation
stage

acute

rapidly deteriorating

death weeks → months

(Bad)

موت سريع

Chronic

mature
(cyte)

gradual
slowly deteriorating

death months → years

(Better)

لذلك لا نقول
Acute بل
يتميز

lymphatic myeloid

lymphoblastic

cyte addi -
chronic = مزمن

Predisposing factors include:

- Genetic: incidence in identical twins & in chromosomal disorders
- Environmental: Ionization, Chemicals as Benzene
- Viral infection: HTLV-1, EBV
- Pre-existing disorders: PNH, MDS

CLASSIFICATION

1. According to the clinical course:

- Acute leukemia: characterized by proliferation of IMMATURE CELLS = BLAST
- Chronic leukemia: characterized by proliferation of MATURE CELLS = CYTE

2. According to the cell type:

- Lymphatic leukemia: from Lymphocytes
- Myeloid leukemia: from Myelocytes

INCIDENCE

[Lymphatic & myeloid leukemia] are nearly of equal incidence

Age: leukemia may affect any age. HOWEVER:

- ALL: more common in children
- AML: more common in adults
- CLL: more common in old age

[myeloid leukemia]

Lymphatic
Lymphoblastic

ACUTE LEUKEMIA

Written
SQ LQ

45

INCIDENCE

- ALL: more common in children & young adults.
- AML: more common in adults.

CLINICAL PICTURE

A) MANIFESTATIONS OF BM FAILURE

1. Anemia:

- Cause: encroachment on the Red cell precursors in the BM, or due to bleeding.
- Description: rapidly developing, progressive, severe.

2. Bleeding:

- Cause: encroachment on the Platelet precursors in the BM → Thrombocytopenia.
- Description: thrombocytopenic bleeding: "see later".

3. Fever & recurrent infections:

- Cause: non-functioning abnormal WBCs.
- Description: in the form of:
 - i. Common sites of infection: mouth, throat, anorectal region, UTI, lungs, skin.
 - ii. Common organisms:
 - Gm + ve cocci: Staph. aureus.
 - Gm - ve bacilli: Pseudomonas.
 - Fungi: Candida.
 - Viruses: HSV.

العدوى
تزداد
لأن
لا يقومون
بوظيفتهم

ulcers
sore & pharyngitis

مستحولات
بإنتاج خلايا سرطانية
WBCs
عشوائية
تتسبب في
التهابات
كوبس

عالية
Symptomatic

B) MANIFESTATIONS OF ORGAN INFILTRATION

1. Lymphadenopathy:

- Generalized LN: of small or moderate size, especially in ALL.
- Cervical LN: may be markedly enlarged & tender due to oral infection.
- Pressure manifestations: e.g. mediastinal syndrome or obstructive Jaundice.

2. Hepatosplenomegaly.

3. Generalized bone pains & STERNAL TENDERNESS.



general examination
(not local chest exam)

acute sign
expands
B.m.
hyper...
White Knight Love

- leukapheresis
Loi
plasma pheresis
(TTP)
4. **Leukostasis:** = stagnation of abn. leukocytes (malignant cells)
- Occlusion of the microcirculation leading to **Ischemia** in different tissues.
 - It affects different tissues, MAINLY: ears, eyes, brain, lungs, penis

لذلك العلاج من قبل anticancer

5. Other organs affection:

★ CNS

especially in ALL > AML

- Brain: cranial nerve palsies.
- Spinal cord: focal paraplegia.
- Meninges: meningeal irritation.

mechanical #
remove cells from
microcirculation
(leukapheresis)

LUNGS

- Hemoptysis.

KIDNEYS

- Hematuria, ARF.

BONES

- Bony pains & pathological fractures.

JOINTS *

- Joint effusion & arthritis.

GIT

- Ulcers & hemorrhage.

GUMS

- Ulcers & hypertrophy, especially in: Monoblastic leukemia.

SKIN

- Rash & nodules.

SEROUS MEMBRANES

- Pericardial effusion, pleural effusion, ascites.

dry
pericarditis
(malignant)
وتنحسج
effusion

TESTIS

- Testicular swelling,

especially in: ALL.

↑ increases in chemotherapy

C) METABOLIC MANIFESTATIONS

- Hyperuricemia: may lead to urate nephropathy & gouty arthritis.
- Hypokalemia: may occur due to renal tubular defect.
- Hyponatremia: may occur due to "SIADH".

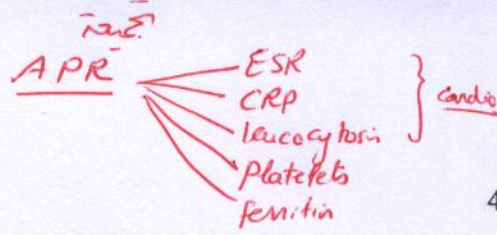
paramalignant
syndrome

↑ tissue damage
(malignant & normal cells)
↓
↑ cells turn over
↓
↑ Ptn break down
↓
↑ Purines (not xanthine)

xanthine
oxidase

↑ U.Acid
بالعش لدر
التي تفرده

Allopurinol
x.o. inhibitor
العلاج
sympomatic



INVESTIGATIONS

1. CBC:

أبدأ بـ RBCs platelets ← حتى لا تنسى

- WBCs: "Leukocytosis"

1. TLC: Increased, may reach 100,000 / cmm.
2. Cells: **BLASTS** are predominant (myeloblasts or lymphoblasts).

3. SPECIFIC TYPES:

- i. Subleukemic leukemia: TLC is normal with presence of: **BLASTS**.
- ii. Aleukemic leukemia: TLC is normal with: **no BLASTS**, in this case the diagnosis depends on BM examination.

	Myeloblasts	Lymphoblasts
Cell morphology		
Cytochemistry	Myeloperoxidase + ve	PAS + ve

محتويات ال cell
تقبل صبغات معينة

- RBCs:

- Normocytic normochromic anemia.

Periodic Acid Schiff : اسفنجية
Glycogen & MPS تصبغ الكبد للأنسجة

oral خيط

Acute phase Reactant (APR) ↑
by tissue damage (acute or chronic)
due to IL-6
Thrombopoietin

- PLATELETS: v. early: Thrombocytosis:

- Thrombocytopenia. encroachment on capacity of fationation (Late)

2. Bone marrow examination:

Host imp

- Hypercellular: infiltrated with sheets of **BLASTS** that replace the normal BM cells.
- BLASTS: more than 30 % & may reach up to 100 % of BM cells.
- BLASTS: myeloblasts or lymphoblasts.

3. Metabolic abnormalities:

- ↑ Serum uric acid: increased.
- ↑ Serum LDH: increased. → non specific → MI, P. Embolism, Hemolysis
- Serum vitamin B12: increased → only in Myeloid not in Lymphatic
- ↓ Serum potassium: may be decreased.
- ↓ Serum sodium: may be decreased. ← tissue damage → ↑ cell turn over & destruction

Hydroxy Cobalamin (B12)

↑ Transcobalamin (comes from White Knight Love from neutrophils)

DIFFERENTIAL DIAGNOSIS

1. CLINICALLY:

Acute leukemia should be differentiated from:

- APLASTIC ANEMIA. (fever, infectn, Bleedg)
- Fever with LN. eg:
- Fever with sore throat. : eg: IMN, Scarlet
- Rheumatic fever. (fever, meningitis, arthritis)
- Miliary TB. (Multiple organ affection) → spill over

2. LEUKEMOID REACTION:

- It is defined as marked leukocytosis ($25,000 / \text{cmm}$) & may be associated with: IMMATURE LEUKOCYTES. but not malignancy criteria (normal)

- Myeloid leukemoid reaction: ($\uparrow$ neutrophils)

• BM infiltration: (myelophthitic anemia).

• BM stimulation: severe Hemolysis, severe Hemorrhage, severe Hypoxia.

- Lymphatic leukemoid reaction: ($\uparrow$ lymphocytes)

Causes:

- Hepatitis.
- HSV, IMN, CMV.
- TB, Brucellosis, Syphilis.

TREATMENT

I. Supportive ttt: (Symptomatic)

1. For anemia: packed red cell transfusion.
2. For bleeding: platelets transfusion.
3. For infections: isolation + antibiotics, antifungal, antiviral drugs.
4. For hyperuricemia: Allopurinol.
5. For leukostasis: Leukapheresis.

II. Specific ttt:

1. Chemotherapy with or without radiotherapy:

A) ALL:

1. Induction of remission: Vincristine⁺, prednisone: for 4 weeks.
2. CNS prophylaxis: Intrathecal methotrexate.
3. Consolidation: Vincristine⁺, prednisone⁺.
4. Maintenance: Vincristine⁺, prednisone⁺, + methotrexate⁺ 6 MP.

B) AML:

1. Induction of remission: Cytosine arabinoside, Daunorubicin: for 7 days.
2. Maintenance: Cytosine arabinoside, Daunorubicin: for 1 year.

2. BMT:

It is indicated in:

- **Progressive:** & refractory cases. (resists chemotherapy)
- **Patients less than:** 45 years.
- **Presence of:** a suitable donor.

Criteria of successful remission:

1. marked improvement of CLP
2. reduction of TLC (eg: 90,000 → 10,000)
3. reduction of Blast Cells

Criteria of cure completely:

1. persistently & repeatedly normal CBC after being abnormal

Alkemia → leukopenia

2. reduction of Blast Cells in BM < 5% (30% → 5%)

Complications of ttt chemotherapy:

1. F.A. ↓↓ (methotrexate & 6MP)

2. ↑↑ U.A. ↑↑ K⁺ → ATLS (Acute Tumor Lysis Syndrome)

MP

phosphorus ↓ و كذلك potassium ↓

Acute hypocalcemia
tetany

ARF occlude tubules

Fatal arrhythmia & may be arrest in diastole

CHRONIC MYELOID LEUKEMIA

Cytes

neutrophils

CLINICAL PICTURE



A) MANIFESTATIONS OF ORGAN INFILTRATION

1. SPLENOMEGALY:

Pain:

- Dragging pain in the left hypochondrium: due to splenomegaly.
- Stitching pain in the left hypochondrium: due to perisplenitis, resulting from splenic infarction (due to leukostasis or thrombosis).

Spleen:

- HUGE size: usually occurs.
- SPLENIC RUB: is usually heard + multiple notches due to infarctions.



Procoagulant factors
abn. activation of clotting factors
Fibrinogen
Fibrin

2. Hepatomegaly:

- The liver may also be enlarged, or even huge, with rounded border.

3. Lymphadenopathy:

- Slight LN enlargement occurs rarely.

lymphatic
اکثر

sharp only 2
Fibrin (B)
cirrhosis

4. Generalized bone pains & STERNAL TENDERNESS.

5. Leukostasis:

- Occlusion of the microcirculation leading to Ischemia in different tissues.
- It affects different tissues, MAINLY: ears, eyes, brain, lungs, penis.

acute
اکثر

6. Other organs affection:

- Leukemic infiltrations of other organs are RARE.

acute
اکثر

B) MANIFESTATIONS OF BM FAILURE

1. Anemia.

Encroachment
Bleeding (↓ platelets)
Hypersplenism
ACD

2. Bleeding. & Thrombosis (OD 5 diseases)

3. Fever & recurrent infections.

C) METABOLIC MANIFESTATIONS

- Hyperuricemia: may lead to urate nephropathy & gouty arthritis.

D) BLAST CRISIS = "Acute on Top of chronic"

- 70 % of the patients will eventually develop transformation into AML.

INVESTIGATIONS

1. CBC:

- WBCs: "Leukocytosis"

- TLC: Increased, may reach 100,000 - 1,000,000 / cmm.
- Cells: MYELOCYTES are predominant with few MYELOBLASTS. MYELOBLASTS increase markedly in Blast crisis.

3. LAP: Decreased.

- RBCs:

- Normocytic normochromic anemia.

- PLATELETS:

- Thrombocytosis, or Thrombocytopenia.

2. Bone marrow examination:

- Hypercellular & full of MYELOCYTES, with few MYELOBLASTS.
- MYELOBLASTS increase markedly in Blast crisis.

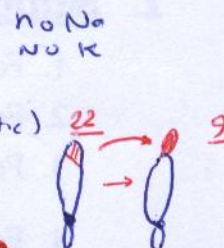
BLAST CRISIS: 30 % or more MYELOBLASTS are present in the BM and / or peripheral blood.

3. Metabolic abnormalities:

- Serum uric acid: increased.
- Serum LDH: increased.
- Serum vitamin B12: increased. (not ↑ in lymphoma)

4. The Philadelphia chromosome:

- Acquired chromosomal abnormality: present in 90 % of patients with CML.
- It results from: translocation of a part of the long arm of chromosome number 22 to the long arm of chromosome number 9.
- It is found in the BM in: granulocyte, erythroid & megakaryocyte precursors.
- Its presence denotes: better prognosis & better response to therapy.



1960
في أمريكا

DIFFERENTIAL DIAGNOSIS

1. CLINICALLY: CML should be differentiated from:

- CLL. : *25%*
- Causes of: **HUGE SPLENOMEGALY** (see later).
- Causes of: **Myeloproliferative disorders:** [abn. proliferation of Bm cells.]
 - CML. *granulocytes (neutrophils)*
 - PRV. *RBCs mainly*
 - *Essential thrombocythemia. platelets*
 - *Idiopathic myelofibrosis. fibroblasts (handrop)*



- ليست كونه في*
- 1 *Huge spleen*
 - 2 *infectn Bleeding anemia*
 - 3 *Thrombosis & Bleeding*

2. LABORATORY: LEUKEMOID REACTION: "see before"

- It is defined as marked leukocytosis (25,000 / cmm) & may be associated with immature leukocytes.
- It is mainly differentiated from CML by:

	Leukomoid reaction	CML
Splenomegaly	Rare	Common
LAP	High	Low
Philadelphia chromosome	Absent	Present in 90 % of cases

Signs of

TREATMENT

I. Supportive ttt:

1. For anemia: packed red cell transfusion.
2. For bleeding: platelets transfusion.
3. For infections: isolation + antibiotics, antifungal, antiviral drugs.
4. For hyperuricemia: Allopurinol.
5. For leukostasis: Leukapheresis.

II. Specific ttt:

1 Busulfan } cytotoxic
 2 Hydroxyurea }
 3 Imatinib } cytostatic

مجرد این دوا به این معنی لوحه
ولا آکیل نه نه نه side effects

1. Chemotherapy:

• **Busulfan:** (Myeleran) 4 – 8 **mg** / day orally

- It should be stopped when TLC is reduced below 25,000 / cmm.
- Side effects: BM failure, pulmonary fibrosis, vomiting & diarrhoea.

• **Hydroxyurea:** 1 – 6 **gm** / day orally

- It has less side effects & better results than Busulfan.

• **Imatinib:** recent drug : 1) ↓ growth of malignant cells (static)
2) inhibits enzyme tyrosine Kinase needed for multiplication

also amiodarone
also anticancer

GIT irritate

2. Interferon – alpha.

3. BMT:

It is the only curative ttt & is indicated in:

- **Progressive:** & refractory cases.
- **Patients less than:** 30 years.
- **Presence of:** a suitable donor.

> 30 graft rejection

4. TTT of Blast crisis:

- TTT is similar to AML but with a poor response.

اشی
1 induction
2 maintenance

1 week
1 year

Interferon normally from WBC lymphocyte

α → not Kill (CML)
but interferes i growth & multiplication

→ antiviral
[HBV
HCV]

B → immunomodulatory in Multiple sclerosis

SCQ نظري

* myeloid : from granulocytes
* lymph : from lymphocyte

B₁₂ ↑ (from neutro + phils)

- Chronic leukemia
نظري

وهذا نظري (لورا جده ص. ٧٠)
مخاطبة قلبه متعلقة

also alveolar = B.C.

also AINA

CHRONIC LYMPHATIC LEUKEMIA

benign cancer : v. low grade

نظري

الحالة بروت عادي
قل قلب بروت منه

- It is the most common form of leukemia in adults especially in: old age.
- CLL is closely related to (and most consider it the same as):
SLL, small lymphocytic lymphoma a type of non-Hodgkin's lymphoma.

النسج لماليم
lymphoid tissue
و نسج بروت
في الغدة
behavior -

CLINICAL PICTURE

1. Asymptomatic: occurs in 25 % of the cases.
نظري لا ملاحظة
inflammatory
2. LYMPHADENOPATHY: "The most important manifestation"
 - Generalized LN: of moderate size, firm, discrete, NOT TENDER.
 - Pressure manifestations: e.g. mediastinal syndrome or obstructive Jaundice.
3. Hepatosplenomegaly.
4. Leukemic infiltrations of other organs may occur.
Leukemic cells نسيج
5. Anemia: due to:
 1. Autoimmune hemolytic anemia (positive Coomb's test).
(warm)
 2. BM infiltration.
 3. Hypersplenism.
 4. - ACD
 5. - Bleeding tendency (↓ platelets)
6. Bleeding: due to thrombocytopenia, due to:
 1. Autoimmune thrombocytopenia. abn. Abs against platelets
نظري
 2. BM infiltration.
 3. Hypersplenism.
7. Fever & recurrent infections. due to abnormal lymphocytes
v. small (immature)
8. Metabolic abnormality:
infection لا تغد، تقادم

NHL is matted
(HL is not matted)

also lymphoma warm

LN
liver
bm
spleen
thymus

خلل في أجزاء الغدة
فنتج
Ab abnormal

Hyper uricemia ← Joint
Kidney

WhiteKnightLove

INVESTIGATIONS

1. CBC:

① - **WBCs:** "Leukocytosis" MAINLY "Lymphocytosis"

- TLC: Increased, may reach 100,000 - 1,000,000 / cmm.
- Cells: SMALL LYMPHOCYTES are predominant.

② - **Hairy cell Leukemia (HCL)** 1. large lymphocyte

- 2. large nucleus
- 3. Hair cytoplasmic projects

③ - **RBCs:**

- Normocytic normochromic anemia.
- Hemolytic anemia: with positive Coomb's test. → warm AIHA (Abs against RBCs)

④ - **PLATELETS:**

- Thrombocytosis, or Thrombocytopenia.

2. Bone marrow examination:

- Hypercellular & full of: SMALL LYMPHOCYTES (> 30 %).

3. Lymph node biopsy:

- Infiltration with: SMALL LYMPHOCYTES.

4. Metabolic abnormalities:

- Serum uric acid: increased.
 - Serum LDH: increased. non specific
- NO B₁₂ (From neutrophils)

DIFFERENTIAL DIAGNOSIS

- CML.
- Causes of: Lymphocytosis. اسبح
- Causes of: Generalized LN enlargement: especially Lymphoma. اسبح

TREATMENT

I. Supportive ttt:

1. For anemia: packed red cell transfusion.
2. For bleeding: platelets transfusion.
3. For infections: isolation + antibiotics, antifungal, antiviral drugs.
4. For hyperuricemia: Allopurinol.

no leukapheresis as no in C/P leukostasis as B-v. not of White Knight Love as small lymphocytes

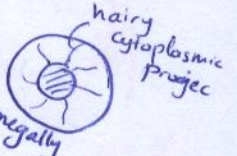
Leukemia جالده واحد
فون 100 ألف على طول

Leukemoid Rx

18

19

الف



II. Specific ttt:

1. Chemotherapy:

- **Chlorambucil:** (leukeran) 0.1 mg / Kg / day orally.
- **Prednisone:** 1 mg / Kg / day orally.

ialio
gene
in
aplastic
anemia

انفرت
فقط في
aplastic
anemia

2. Radiotherapy:

- Irradiation of LN & spleen may be needed.

كماروبينجتوا خلايا سرطانية

POLYCYTHEMIA

DEFINITION

- Increase in red cell mass: $> 36 \text{ ml / Kg in males}$ & $> 32 \text{ ml / Kg in females}$.

Androgen ↑
RBCs

Menstruation ↓
RBCs

ETIOLOGY

A) Secondary polycythemia:

1. **Chronic hypoxia** (e.g. COPD & other causes of chronic central cyanosis).
2. **Cushing's syndrome & prolonged corticosteroid therapy.**
3. **Renal disease** (e.g. hypernephroma & hydronephrosis) → ↑ EPO.
4. **Paramalignant syndrome** (e.g. HCC).
5. **Dehydration** → hemoconcentration (false polycythemia).
6. **Smokers polycythemia:** Nicotine in Blood → ↑ Carboxy Hb → ↓ oxygenated Hb → ↑ EPO

أهم سبب عن إبطاء جريان
النظرية في سبب

cortisol
↑ O₂ needs
↑ RBCs

False
Pregnancy
dilutional
anemia

- ① - not Blood malignancy
- ② - Erythropoietin dependant (Ep dependant)
- ③ - E P ↑
- ④ - Causes → ↑ EP
- ⑤ ↑ only RBCs.
- ⑥ O₂ saturation → Low (if cause hypoxia)

SLE
B.A.

Mass compression on Renal vessels → ↓ Blood as if ischemia

15% Liver
85% Kid
rr

B) Polycythemia Rubra Vera:

"PRV"



- A myeloproliferative disorder (blood malignancy) characterized by:

"Excessive proliferation of"

- | | | | |
|----------------------|---|-------------|--------------------------|
| ERYTHROIDS in BM | → | ↑ RBCs | in the peripheral blood. |
| MYELOIDS in BM | → | ↑ WBCs | in the peripheral blood. |
| MEGAKARYOCYTES in BM | → | ↑ Platelets | in the peripheral blood. |

④ no cause

⑤ ↑ all mainly RBCs

⑥ Normal O₂ Saturation

Normal
↓ (-ve
feed
back)

abn.
proliferate
of B.m. cells
mainly RBCs
(not only)

Epo لا يفرز Normal لا يفرز ← Cancer → polycythemia

White Knight Love

CLINICAL PICTURE

1. Plethoric appearance.

وش أحمر

2. Symptoms due to Hyperviscosity: "Circulation slow"

- Neurological: headache, dizziness, tinnitus, blurring of vision, parasthesias.
- CVS: dyspnea, palpitation, precipitation of angina.
- EYE: conjunctival suffusion, retinal venous engorgement.

anemia
↓ viscosity
↓ hypodynamic

3. In PRV:

- MANIFESTATIONS:

- Hepatomegaly.
- SPLENOMEGALY: HUGE size.
- Peptic ulcer: ↑ HCL due to associated increase in Histamine level.
- Pruritus. ↑ Histamine From Basophils & Mast cells → Irritation to skin receptors generalized itching

due to infiltration
due to infiltration & enlarged to destroy cells

- COMPLICATIONS:

- Vascular thrombosis: e.g. Stroke.
- Bleeding tendency. e.g. Stroke.
- Hypertension.
- Hyperuricemia.

↑ viscosity
↑ Procoagulant
↑ viscosity

tissue damage
↓ Xanthine
↓ U.A.

as of:
anemia
↓ COP

4. In secondary polycythemia:

- Features of the cause. eg: COPD

symp. of chronic Bronchitis
sign: Hyperinflated chest wheezing
cough + mucoid sputum
cough + mucopurulent
Dyspnea + wheezing

INVESTIGATIONS

1. CBC:

- RBCs:
 - Increased number (above 6 million / cmm).
- WBCs:
 - Increased number (above 12,000 / cmm).
- PLATELETS:
 - Increased number (above 400,000 / cmm).

in 2ry [only RBCs ↑] EPO ↑

oral
Causing generalized pruritus
① Histamine → PRV allergic
② Bile Salts → obstructive & Hepatocellular jaundice
③ ↑ Glucose → DM
④ Uremia & toxins
⑤ Calcium in Hyperparathyroid

In PRV ONLY

2. Bone marrow examination:

- HYPERCELLULARITY of ALL bone marrow elements.

In PRV ONLY

ii

RBCs

in

2ry only

3. ESR: Low.

4. Red cell mass:

- Increased: $> 36 \text{ ml / Kg in males}$ & $> 32 \text{ ml / Kg in females}$.

5. Tests to differentiate between Secondary polycythemia & PRV:

a. Arterial blood gases: $O_2 \text{ saturation}$

- In secondary polycythemia: Decreased oxygen saturation.
- In PRV: Normal oxygen saturation.

b. Serum EPO:

- In secondary polycythemia: Increased.
- In PRV: Normal or low.

6. Others:

- Serum uric acid: increased.
- Serum LAP: increased.
- Serum vitamin B12: increased.

neutrophils spike of WBCs & also Cancer cell

DIAGNOSIS OF PRV

A

A1: Increased Red cell mass: $> 36 \text{ ml / Kg in } \sigma$ & $> 32 \text{ ml / Kg in } \phi$.

A2: Normal oxygen saturation.

A3: Splenomegaly. huge

B

B1: Increased Platelets: $> 400,000 / \text{cmm}$.

B2: Increased WBCs: $> 12,000 / \text{cmm}$.

B3: Increased LAP.

B4: Increased serum vitamin B12.

- DIAGNOSIS is established if the following combinations are present:

- A1 + A2 + A3, or:
- A1 + A2 + any 2 from category B.

PRV
A & B

Oral indicates if repeated venesection

uses of Hydroxyurea

1. hemoglobinopathies
2. Myeloproliferative

1. Refl. H.F.
2. A.cute
3. Polycythemia
4. Hemochromatosis

59

TREATMENT

A) PRV

1. Repeated venesection: to keep the Hematocrit value in the range of **45 %**.
*جل دم منه
لأنه عند دم
زيادة*
2. Chemotherapy:
 - Hydroxyurea: is the best.
 - Radioactive phosphorus: Busulphan: may be used.
3. TTT of complications: HTN → proper control
Hyperuricemia → Allopurinol

B) Secondary polycythemia:

1. Repeated venesection: to keep the Hematocrit value in the range of **45 %**.
جل دم منه
2. TTT of the cause. eg COPD

IDIOPATHIC MYELOFIBROSIS

= Myelo Sclerosis

hard
B.m. ليف
الليف
Semiliquid

DEFINITION

- Progressive generalized fibrosis of the BM, associated with:
- Haemopoiesis in the *liver & spleen* (known as: Myeloid Metaplasia).

المخارج
الحساب
المتقل

ETIOLOGY

UNKNOWN

EARLY Idiopathic abnormal change in the stem cell in the BM leading to:

- Decreased production of: RBCs.
- Increased production of: WBCs.
- Increased production of: abnormal MEGAKARYOCYTES.
- Abnormal Megakaryocytes secrete: GROWTH FACTORS.
- Growth factors stimulate: FIBROBLASTS to produce fibrosis of BM.

w Bcs, platelets
زيادة
ووجه

early

انفرا

LATE

Excessive BM fibrosis will ↓↓ the ability of the BM to make blood cells:
→ Decreased all blood cells → PANCYTOPENIA.

BM ليف

CLINICAL PICTURE

- | | |
|-------------------------|-----------------------------------|
| 1. Decreased RBCs: | General manifestations of anemia. |
| 2. Decreased WBCs: | Fever & recurrent infections. |
| 3. Decreased platelets: | Purpura & bleeding tendency. |



4. SPLENOMEGALY: HUGE size.
5. Hepatomegaly: Mild.

6. Thrombosis (malignancy of blood → procoagulant factors)

INVESTIGATIONS

1. CBC:

“Pancytopenia”

- RBCs: Normocytic normochromic anemia: with teardrop RBCs.
- WBCs: Early Leukocytosis, → Late Leukopenia.
- PLATELETS: Early Thrombocytosis, → Late Thrombocytopenia.

2. Bone marrow examination:

“Aspiration & biopsy”

- Aspiration: BM specimen cannot be obtained.
- Biopsy: Fibrotic BM.

DIFFERENTIAL DIAGNOSIS

- | | |
|---------------------|--------------------------------------|
| 1. Other causes of: | <u>PANCYTOPENIA.</u> |
| 2. Other causes of: | <u>HUGE SPLENOMEGALY.</u> |
| 3. Other causes of: | <u>Myeloproliferative disorders.</u> |

TREATMENT

I. Supportive TTT:

- For deficient blood cells: Repeated Blood transfusion.
- For splenomegaly: Splenectomy or radiotherapy (spleen shrinkage)

II. Specific TTT:

1. Chemotherapy:

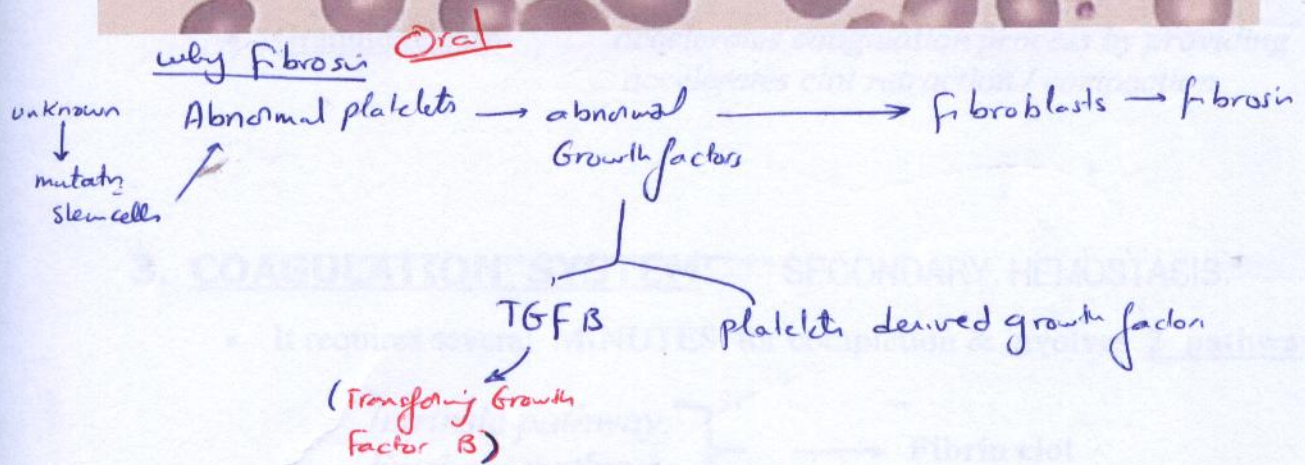
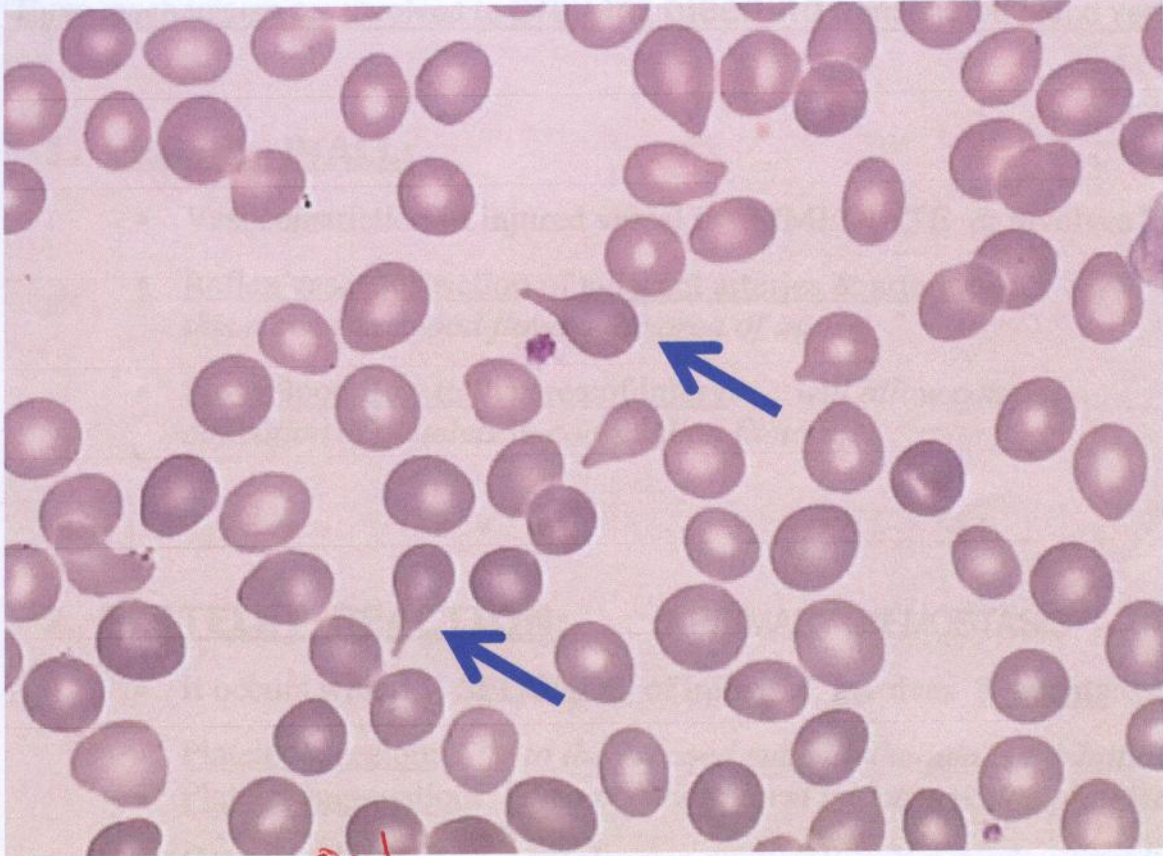
- Hydroxyurea.

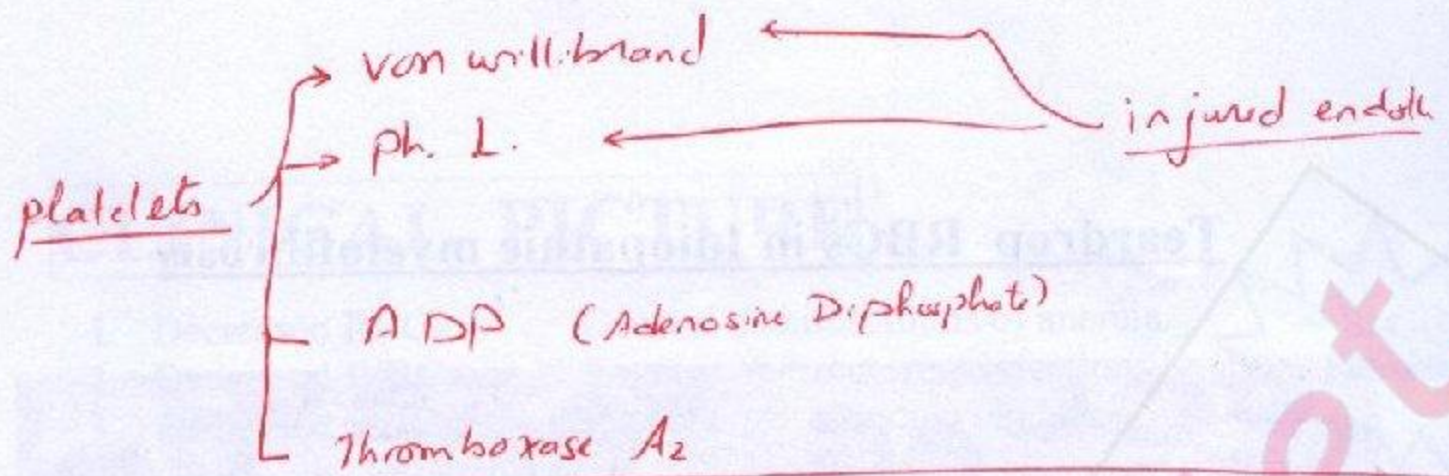
2. Stem cell transplantation:

- It is the only hope for cure.

or whole B.m. Transplantation

Teardrop RBCs in Idiopathic myelofibrosis





NB.

if abn. vessel wall or platelets → purpura → نزف في جال immediate
(normal coag. factors)

if abn. coag. factors → hemophilia → نزف متأخر وبعده
(normal vessel wall & platelets) كل دقيقة لأنه فيه حاجة سد مؤقتاً (platelets plug)

NB

after platelets make clot

the clots must be lysed to allow blood flow to be normal

وهذا بعمل تفكيك لل Fibrin الذي هو الذي ملأه الجلطة

by fibrin lysis (fibrinolytic system) ← plasmin plasminogen Activator

وهي وظيفة أجلة انه فتح جدران غريبة من غير جروح في حالات Hypercoagulable

NB

* extrinsic → both are each other for clotting

* intrinsic

but extrinsic is activation of clotting from without
but intrinsic " " " " with a

• platelets → Bleed Time ↑ & rest normal

• ↓ factor 7 →

①	BT	
②	CT	↑
③	PT	↑
④	APTT	±
⑤	TT	↑

= arrest of bleeding

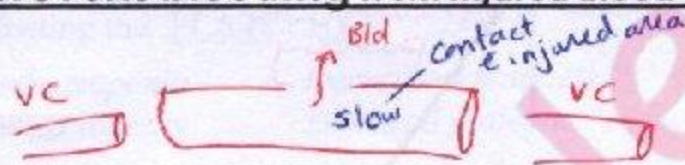
NORMAL HEMOSTASIS

از ای توقف انزیم

لستغلوا تباعاً مش مع بعضه

Three mechanisms are involved to prevent bleeding from injured blood vessels:

وكل خطوة تعمل الى على مساعد الى بعدها



1. VESSEL WALL:

- Vasoconstriction of injured vessel is IMMEDIATE & involves 2 events:
- Reflex vasoconstriction of adjacent arteries & arterioles: *this slows the blood flow to the area of injury.*
- Slow blood flow to the area of injury: will allow contact activation of platelets & coagulation factors...

توقف انزيم

يساعد الانزيم الى بعدها

= platelets

2. PLATELET REACTION:

صياوح قوتى

"PRIMARY HEMOSTASIS"

by bridges (von willebrand factor) from injured endothelium

- It occurs within SECONDS of injury & involves 3 events:
- Platelet adhesion: to the exposed subendothelium is the initial response.
- Platelet aggregation: then occurs to form the obstructing platelet plug.

1 - adhesion
2 - helps factor VIII

- Granule release:

accelerates coagulation process by providing Ph L. accelerates clot retraction / compaction.



clutch fibrin w approximate ends of endothelium

متأخر شوية

تكرير

phospholipids accelerate clotting system

3. COAGULATION SYSTEM: "SECONDARY HEMOSTASIS"

- It requires several MINUTES for completion & involves 2 pathways:

- Intrinsic pathway.
- Extrinsic pathway. } → Fibrin clot

oral

ph. lipid
طرح مينه
granule release by platelets

منه اخرى من endothelium

زي قمره von willebrand

- platelet
- endothelium

White Knight Love

platelets plug → compact clot

COAGULATION PATHWAYS

EXTRINSIC PATHWAY

= Tissue Factor Pathway

Tissue injury

Tissue factor (from adventitia of BVs) & from perivascular tissue

= III

+ Ca + Ph L from platelets & injured endothelium

7

= Complex
Thromboplastin
= TF + Ph. L.

INTRINSIC PATHWAY

= Contact activating Pathway

Contact with vascular subendothelium

12

+ HMWK & PK

11

+ Ca + Ph L

9

+ Ca + Ph L + 8

10 Common Pathway

+ 5 + Ca + Ph L

2 (Prothrombin)

Thrombin

1 (Fibrinogen)

Fibrin

Fibrin stabilizing factor

13

CLOT

8 ↓ hemophilia A
9 ↓ " B

Oral T.F. Released from all tissues
brain lung placenta
تفرغ من كل أنسجة في الجسم

نسفي
hemophilia
purpura
ويبقى به نخري

GENERAL TESTS FOR HEMOSTASIS

نسيج
مالوش
أعلاقة
أبدا
Clothing
Pathways

1. BLEEDING TIME BT (2-7 minutes)

- Normally: It measures platelet plug formation.
- Prolonged: Diseases affecting the PLATELETS:
 - Thrombocytopenia "Decreased platelets" No ↓
 - Thrombocytopathy "Diseased platelets" Fm ↓

نسيج و تقطع نخاع
اللكة لخاية ما تبص تلاق
مفيسي دم طالع

نسيج
مالوش
علاقة
أبدا
platelets
Fbrin

2. COAGULATION TIME CT (5-10 minutes)

- Normally: It measures coagulation function (coagulation factors).
- Prolonged: All types of COAGULATION disorders.

نقص دم على ازالة
و تقطع نخاع
بارة لخاية ما يكون
خيط (fibrin)
↓ invivo

نسيج
مالوش
علاقة
بال
intrinsic
خاتما

3. PROTHROMBIN TIME PT (12-14 seconds)

- Normally: It measures the function of the extrinsic & common pathways. It is measured by: adding Tissue factor + Ca + PhL to the plasma and measuring the time to clot formation.

- Prolonged: Diseases of both the extrinsic & common pathways:
 - Diminished factors: 7, 10, 5, 2, 1.
 - Liver cell failure.
 - Vitamin K deficiency (OJ, oral anticoag, malabsorption syndrome).

انت بتعمل heparin
من نخاع
من قتل
heparin
by CT

LCF (hepatocellular jaundice)
+ vit K
ملو عصبية
vit K لا يتفرغ لانه الحب
في النسيج

4. ACTIVATED PARTIAL THROMBOPLASTIN TIME APTT (30-40 seconds)

- Normally: It measures the function of the intrinsic & common pathways. It is measured by: adding Kaolin + Ca + PhL to the plasma and measuring the time to clot formation.

- Prolonged: Diseases of both the intrinsic & common pathways:
 - Diminished factors: 12, 11, 9, 8, 10, 5, 2, 1.
 - Liver cell failure

oral anti coag
inhibits
vit K dependent
Factors
2, 7, 9, 10
لانه لو تبص العنبر
oral anti coag
تأخر
PT

Oral
difference between
H.C jaundice & O.Jaundice.

5. THROMBIN TIME TT (9-11 seconds)

- Normally: It measures the ability to convert Fibrinogen to Fibrin. It is measured by: adding Thrombin to the plasma and measuring the time to clot formation.

- Prolonged: Diseases affecting FIBRINOGEN:
 - Fibrinogen deficiency (afibrinogenemia).
 - Fibrinogen dysfunction (dysfibrinogenemia).
 - Fibrinogen inhibitors (patients on heparin).
 - DIC.

NB
INR: International
normalized
ratio
PT (patient)
PT (control)
normally = $\frac{12 \text{ sec}}{12 \text{ sec}} = 1$
if PTT
INR
abnormally > 1

يحببت
للحاج
vit K
يحببت
للحاج
vit K
فبرين
فبرين

Controlled
by INR
oral anticoag
White Knight Love

Oral type Drug induced purpura?

HEMOSTATIC DISORDERS

TYPES

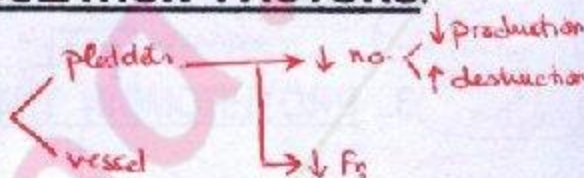
I. PURPURA

- Bleeding tendency due to defects in PLATELETS or in VESSEL WALL.

II. COAGULOPATHY

- Bleeding tendency due to defects in COAGULATION FACTORS.

I. PURPURA



A) PLATELET DEFECT

1. Thrombocytopenia:

"Decreased platelets"

a) Decreased platelet production:

- Bone marrow failure.
- Bone marrow infiltration.
- Megaloblastic anemia.
- Myelodysplastic syndromes.
- PAROXYSMAL NOCTURNAL HEMOGLOBINURIA. associated B-H hypoplasia

b) Increased platelet destruction:

- Autoimmune: Primary (ITP), Secondary (SLE, CLL, Lymphoma, drugs as α-meth-d).
- Acute infections.
- Hypersplenism.
- DIC, TTP, HUS.

as in MAHA

autoimmune thrombocytopenic purpura

في

يكسر

خبط وفقد في الدم

consumptive

as MAHA HA

2. Thrombocytopathy:

"Diseased platelets"

a) Hereditary:

e.g. Glanzmann's disease: ↓ platelets aggregation

b) Acquired:

- Uremia. R.F. toxins → coat platelets
- Multiple myeloma. abn. globulins → coat platelets
- Thrombocytosis. Cancer of platelets (↓ F₈) abnormal
- Antiplatelet drugs: aspirin, dipyridamole, ticlopidine.
- Autoimmune:

SLE. how? causes purpura

↓ No
↓ F₈ (Abs)

breaks B.v. by vasculitis

في
الدم
كثير
وغير
normal

also
CAD

بالفشل القلبي
(فشل)
↓ F₈

WhiteKnightLove

B) VESSEL WALL DEFECT

(Vascular Purpura)

- **Immune:** Vasculitis e.g. SLE, PAN, Henoch-Schonlein purpura.
- **Infection:** SBE, meningococemia. *final destination is cross BBB but began by nasopharynx*
- **Iatrogenic:** Salicylates, Sulphonamides, Penicillins, Corticosteroids. *unknown maybe hypersensitivity*
- **Idiopathic:** Purpura simplex.
- **Scurvy.** $\downarrow$ vit C $\bar{u}$ is needed for collagen (in B.v. wall) $\bar{u}$ needed for adhesion of platelets
- **Senile purpura.** $\bar{e}$ Aging $\rightarrow$ Collagen degeneration.
- **Cushing's syndrome.** $\uparrow$ cortisol $\rightarrow$ catabolic on ptn (collagen) $\rightarrow$ stria rubra
- **Congenital:** Ehlers-Danlos syndrome. weakness of C.T. of B.v. wall

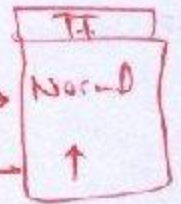
2 diabetes mellitus on CHD

4 mobilization of fat $\rightarrow$ moon face buffalo hump

II. COAGULOPATHY

A) HEREDITARY

- Hemophilia. *A B*
- Fibrinogen defect: Afibrinogenemia, Dysfibrinogenemia. *$\downarrow$ Quantity $\downarrow$ Quality*



B) ACQUIRED

- **Liver failure.** $\downarrow$ conversion of vit K $\rightarrow$ clotting factors & platelets
- **Renal failure.** *Toxins cause clotting factor*
- **Deficiency of vitamin K.**
- **DIC.** *consumption of clotting factors & platelets*
- **Drugs:** Heparin, oral anticoagulants, fibrinolytic agents.

*التقريب
أدى
Parenteral
vit K
الاحتياج ببطء
 $\downarrow$ vit K*

CLINICAL PICTURE

I. BLEEDING:

A) In Purpura:

1. Site of bleeding:

- **Orificial:** epistaxis, melen, Hematochezia, Hematemesis, Hemoptysis, Hematuria.
- **Cutaneous:** petichae, ecchymosis, excessive bleeding from wounds, +ve Hess test.
- **MM:** oral, gingival, conjunctival.
- **Internal:** intracranial hge, retinal hge, cavitary hge (serous membranes).

2. Mechanism of bleeding:

- **Bleeding:** spontaneous or post-traumatic.

3. Character of bleeding:

- **Bleeding:** immediate.

*from upper GIT
 $\rightarrow$ rectum*

*from lower GIT (fresh blood)
 $\rightarrow$ rectum*

*platelets
clotting factors*

*[1] MI
[2] Pulm. Emb*

*intra v. infra minor trauma
جلد و جف*

B) In Coagulopathy:

1. Site of bleeding:

- Orificial: epistaxis, melena, Hematochezia, Hematemesis, Hemoptysis, Hematuria.
- Cutaneous: petichae, ecchymosis, excessive bleeding from wounds, -ve Hess test.
- MM: oral, gingival, conjunctival.
- Internal: hemarthrosis, muscle hematoma, others like in purpura.

2. Mechanism of bleeding:

- Bleeding: spontaneous or post-traumatic.

intra cranial
retinal
intra cavity

3. Character of bleeding:

- Bleeding: delayed.

II. ANEMIA:

- Acute & chronic post-hemorrhagic anemia may occur.

III. SHOCK:

- Severe hemorrhage may lead to: hypovolemia & shock.

IV. MANIFESTATIONS OF THE CAUSE.

Hess test (capillary fragility test)

Method: A circle 5 cm in diameter is marked on the antecubital fossa. The Sphygmomanometer is inflated to midway between SBP & DBP for 5 minutes. Count the number of petichae within the circle.

Result: Positive test means the presence of more than 10 petichae.

Value: It is POSITIVE in all cases of purpura

not
investigations
but bedside
clinical test

Tests

• B.v. Collagen

• Platelets: adhesion & aggregation

INVESTIGATIONS

A) Screening investigations:

- GENERAL TESTS FOR HEMOSTASIS.

B) Specific investigations:

1. PLATELETS:

- Platelet count: Decreased in thrombocytopenia. $< 150,000$
- Platelet function tests: to estimate platelet aggregation by platelet aggregometer

2. CBC:

- May detect the cause of thrombocytopenia (e.g. leukemia).

3. BM examination:

- May detect the cause of thrombocytopenia (e.g. aplastic anemia).

4. ASSAY:

- Coagulation factors assay, FDPs assay.

eg: ↓ Factor 8 - Hemophilia A

↑ in DIC

Clotting
factors

immune

IDIOPATHIC THROMBOCYTOPENIC PURPURA

1 ETIOLOGY

try autoimmune ↑ destruction platelets

- It is an autoimmune disease in which **antiplatelet antibodies** (usually IgG).
- These autoantibodies directed against **glycoprotein IIb / IIIa** of the platelets, will **sensitize** the platelets resulting in their premature **removal** from the circulation by macrophages of the **RES**, especially the **SPLEEN**.
- The life span of platelets is reduced to **few hours** (normally: **7 days**).

2 CLINICAL TYPES

I. ACUTE ITP

"2 types"

- ① **Age:** children.
- ② **Sex:** equal.
- ③ **Onset:** acute.
- ④ **Course:** severe.

- 90%: **resolve** spontaneously within **2 weeks to 6 months**.
- 10%: develop **chronic ITP** (lasting > 6 months).

- ③ **CP:** see before.

④ Investigations:

- ① Platelets: **markedly ↓↓** (usually below **20,000 / cmm**).
- ② BT: **prolonged.**
- ③ CT: **normal.**
- ④ PT: **normal.**
- ⑤ APFT: **normal.**
- ⑥ TT: **normal.**

- **BM examination:** increased number & size of megakaryocytes with: **"defective budding"**.

- **Antiplatelet antibodies:** **Antiglycoprotein IIb / IIIa** antibodies are detected.

⑤ Treatment:

1. General measures:

- **Avoid:**

2. Specific measures:

- **Prednisone:** **1 mg / Kg / day.**
- **Platelet transfusion:** in cases of **severe hemorrhage.**
- **IV gamma globulins.**

V.V.V. effective

trauma, invasive procedures, antiplatelets, eg aspirin

1 mg / Kg / day.

in cases of severe hemorrhage.

Block site of binding on Macrophages to platelets

↓ synthesis of Abs



منه من رطب
الحاج على
spleen

IgG also
paroxysmal
cold
hemoglobinuria

eg.
also Hepatitis
<6M >6M
Acute Chronic
eg
chronic
<1M >1M
Acute Chronic

as immature (large)

platelet in BM

= megakaryocyte

ولا تتكاثر
budd

White Knight Love

N.B. coronary/stroke of Sr. → ♂

N.B. autoimmune → ♀ except (PAN in ♂)

II. CHRONIC ITP

also ^{refers to} autoimmune angitis
D.S. = MS
(Disseminated Multiple sclerosis)

①

Age: young adults & middle age.

Sex: more common in females.

②

Onset: gradual. / mild

Course:

○ Prolonged for: months or years with remissions & exacerbations.

③

CP: see before.

④

Investigations:

- ①
- Platelets: moderately ↓↓ (usually 20,000 – 100,000 / cmm).
 - BT: prolonged.
 - CT: normal.
 - PT: normal.
 - APTT: normal.
 - TT: normal.

② **BM examination:** increased number & size of megakaryocytes with: "defective budding".

③ **Antiplatelet antibodies:** Antiglycoprotein IIb / IIIa antibodies are detected.

⑤

Treatment:

1. General measures:

- Avoid: trauma, invasive procedures, antiplatelets.

2. Specific measures:

• Prednisone:

1 mg / Kg / day.

• If no response:

• If no response:

- Immunosuppressives:

- Danazol.

Androgen

Cyclophosphamide or Cyclosporin.

immunosuppressive drugs.

• Platelet transfusion:

in cases of severe hemorrhage.

• IV gamma globulins.

Oral

unknown unexplained
✓ effective ++ platelets
but side effect: Androgen = ♀
أي أنه لا يوصى به

أدوية نائف

HEMOPHILIA

① ETIOLOGY

- It is a hereditary deficiency of AHG (factor VIII) transmitted as X-linked from healthy female carriers to their male offsprings.

2 CLINICAL PICTURE

Age:

Sex:

Family history:

CP:

since birth.

males.

positive.

see before.

Bleeds - Birth

 $A(z)$

B (9)

Christmas

(AHG) → Anti Hemophilic globulin
Christmas

اس طرح
CLP

- Hemophilia
- G6PD
- Duchenne

hereditary disease
presents
on 40-50 y
↓
Huntington
Chorea

3 INVESTIGATIONS

- | | | | |
|--------------------|--------------------------|---------------------|-----|
| 1. CT: | <i>All</i> | prolonged. | ↑ |
| 2. APTT: | <i>intrinsic & g</i> | prolonged. | |
| 3. TT: | | normal. ✓ | } ✓ |
| 4. PT: | | normal. ✓ | |
| 5. BT: | | normal. ✓ | |
| 6. Platelet count: | | normal. | ✓ |
| 7. Serum AHG: | <i>VIII</i> | markedly decreased. | |

Coagulation Assay

18 is A
19 is B

④ TREATMENT

- ### 1. General measures:

avoid: *trauma, invasive procedures, antiplatelets.*

- ## 2. Specific measures:

“ttt of bleeding episodes”

1. Factor VIII replacement.
2. Fresh blood transfusion:
3. Local pressure →
- For hemarthrosis:

factor VIII concentrates, fresh frozen plasma.
in cases of severe hemorrhage.

immobilization, elastic bandage, analgesics, physiotherapy.

لا احرز
وامنهم علي

تذکرہ کتاب معجز / ہرج / ماسک این بیدہ کاریمہ فیصلہ ایم
عاشقہ یوسفزادہ اللہ ربا
ہمارا 3 جلد
hemorrhoid 14-204

hemorrhoids 14-20y

D.D. of purpura
D.D. of Hemophilia

	Purpura	Hemophilia
1. FH	Negative	Positive
2. Sex	Females mainly	Males only
3. Age	Any age	Since birth
4. Relation to trauma	Immediate	Delayed
5. Hemarthrosis	Uncommon	Common
6. Hess test	Positive	Negative
7. INVESTIGATIONS		

- BT
- CT
- APTT
- Platelets

- Prolonged
- Normal
- Normal
- Low

* anti pl. Abs
* Mega & def. body

- Normal
- Prolonged All intrinsic
- Prolonged
- Normal
- ↓ VIII

Hypoprothrombinemia

factor 2

S.Q. v. short

ETIOLOGY

Can't convert K → prothrombin
(vit K not improved)

1. Liver cell failure → vit K improves it parentally
2. Vitamin K deficiency: OJ, Oral anticoagulants, Malabsorption syndrome.
3. Hereditary deficiency of prothrombin: RARE.
4. Oral anticoag. : inhibits vit K dependent factors 2, 7, 9, 10

CLINICAL PRESENTATION

- Bleeding tendency: especially post-traumatic.
- CP of the cause: most important features of each cause.

e.g. Features of liver cell failure:

INVESTIGATIONS

1. APTT is prolonged. intrinsic
2. PT is prolonged & improves by parenteral vitamin K in cases of vitamin K deficiency ONLY. PT is prolonged but does not improve by parenteral vitamin K in cases of liver cell failure.
3. TT is normal. fibrinogen

Investigations for the cause: most important investigations of each cause.

e.g. Hypoalbuminemia in liver cell failure / Malabsorption urinary-D. xylose test

TREATMENT

1. Transfusion of: fresh frozen plasma. or factor II
2. Treatment of: the cause: e.g. ttt of liver cell failure.
3. Treatment with: parenteral vitamin K in cases of vitamin K deficiency.

OJ Malabsorption

platelets:

causal factors
HCA & PR
& Oral

150 - 400,000

Normally: no bleeding

100 - 150,000

No bleeding

لا يوجد
لوقل
100

50 - 100,000

Bleeds on severe trauma

20 - 50,000

" " Mild "

10 - 20,000

Spontaneous bleeding

<10,000

threatening of life of pt → (ICH)

أي واحد طبيعي
هناك مع فج
من هنا يكون

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HENOCH-SCHONLEIN PURPURA

1. ETIOLOGY

- It usually follows a:
- It usually affects:

STREPTOCOCCAL INFECTION.
CHILDREN.

also
Strept
↓
Autism
- RF
- GN

2. CLINICAL PICTURE

- | | |
|------------|---|
| 1. Blood: | Purpura. |
| 2. Joints: | Arthralgias. |
| 3. GIT: | Abdominal colics, Melena, Hematochezia. |
| 4. Renal: | Hematuria, GN, Renal failure. |

upper GIT

arthralgia
mainly

arthralgia

lower GIT

also
SLE
↓
both
arthralgia
& arthritis
but mainly
-algia
والفرد هو
imitation
of mvt.

3. TREATMENT

- Corticosteroids: prednisone 1 mg / Kg / day orally.

PRV

1y
2y

THROMBOCYTOSIS

= Thrombocythemia

ISQ

1. ESSENTIAL THROMBOCYTOSIS

"PRIMARY"

Definition

- A) It is a myeloproliferative disorder (Blood malignancy) characterized by:
"Excessive proliferation of"

MEGAKARYOCYTES in BM → ↑↑ Platelets in the peripheral blood.

- B) It also occurs in other forms of MPD: CML, PRV, Idiopathic myelofibrosis.

MPD
- CML
- IMF
- PRV
- ...

2. CLINICAL PICTURE

1. THROMBOSIS. Malignancy →
2. BLEEDING. ↑ No but abn. fn → leuko-agreg. ↑ but abn. -agreg.

- ③ SPLENOMEGALY: HUGE size. in all MPD

spleen infiltrated
spleen destroys ↑ No

3. INVESTIGATIONS

1. Platelet count: persistently greater than 1,000,000 / cmm.
2. Bone marrow: marked Hypercellularity of Megakaryocytes.

H.U. in MPD
- Hemoglobinopathies

A TREATMENT

1. Chemotherapy: Hydroxyurea, Radioactive phosphorus.
2. Symptomatic ttt: Platelet-pheresis.

also
- PRV

2. REACTIVE THROMBOCYTOSIS "SECONDARY"

- It is more common than essential thrombocythosis.
- Causes include:

- Inflammation.
- Infection.
- Malignancy.
- Hemorrhage.
- POST-SPLENECTOMY.

investig.

platelets 700,000

as
↑APR
(platelets)

by IL-6
& Thrombopoietin

- 50,000 Thrombocytopenia
- 300,000 Normal
- 2,000,000 1ry
- 700,000 2ry

(DIC) تفصيل

Causes (esp. sepsis)

endothelial injury (torn)

tissue injury

Injury → cytokines
Procoagulant ← TNFα

rough surface (contact) platelets intrinsic

Thrombosis*

wide spread
Abn. clotting

adventitia
perivascular tissue

rough endoth
mechanical
destructive

Consumption

platelets
clotting factors

Bleeding*

↑ activation of
fibrinolytic system
کود فیل فایبرین
فایبرین
فایبرین

platelets
RBCs
MAHA (C/P of H.A.)
(investig: schistocytes)

HYPERSPLENISM

DEFINITION

- Exaggeration of the normal splenic function → destruction of one or more of the blood cells:
"Monocytopenia, or Bicytopenia, or Pancytopenia".

ETIOLOGY

1. Secondary: Splenomegaly.
2. Idiopathic: Rare.

CLINICAL PICTURE

1. One or more of the following:
 - Anemia: RBCs.
 - Bleeding: PLATELETS.
 - Fever & recurrent infections: WBCs.
2. Splenomegaly: + features of the cause of splenomegaly.

eg: PH esp β, cirrhosis
esoph. varices

INVESTIGATIONS

1. CBC: One or more of the following:

Hemolytic Anemia →

- RBCs: Normocytic normochromic anemia, with reticulocytosis.
- PLATELETS: Thrombocytopenia.
- WBCs: Leukopenia.

2. Bone marrow examination: Hyperplasia.

3. Cr. Labeled RBCs: excessive destruction in the spleen.

4. Investigations for the cause of splenomegaly.

- W/S
- Cause: Anti-schistosomal Abs.

TREATMENT

1. SPLENECTOMY.
2. Symptomatic ttt: for anemia, bleeding, infections.
3. TTT of the cause.

انسجی لیکن

QUESTION 1

- A ♂ patient, 37 years old with huge splenomegaly:
 - o Hb: 8 gm %
 - o WBCs: 117,000 / cmm
 - o Platelets: 124,000 / cmm
- Mention the 2 most probable possibilities.
- Mention one most important investigation at this point.

Answer:

- CML, IMF (early)
- BM

QUESTION 2

Anemia of uremia:

- a) Is always NN. F
- b) Is treated with recombinant EPO. T
- c) Is treated with G-CSF. F
- d) Is associated with thrombocytopenia. F
- e) Is caused by BM calcification. T

QUESTION 3

Hemolysis:

- a) Is a complication of CLL. T
- b) Occurs during CP of Malaria. T
- c) Occurs during ttt of Malaria. T
- d) Occurs due to EBV, HBV, HCV. T
- e) Is associated with hyperplastic BM. T

QUESTION 4

In liver cell failure:

- a) PT is prolonged. T
- b) APTT is prolonged. T
- c) BT is prolonged. T
- d) TT is prolonged. T
- e) CT is prolonged. T

QUESTION 5

Platelets:

- a) Have a life span of 10 hours. F
- b) Are produced & regulated by thrombopoietins. T
- c) Contain small nuclear remnants (Howell-Jolly bodies). F
- d) Decrease in number in response to aspirin therapy. F
- e) Release serotonin & Thromboxanes. T

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QUESTION 6

Hemolytic anemia may be associated with:

- a) Jaundice. T
- b) Impotence. T
- c) Oedema LLs. T
- d) Central cyanosis . F
- e) Flapping tremors. T

QUESTION 7

- A ♀ patient, 45 years old presented with anemia:

- o Hb: 7 gm %
- o Serum iron: ↑
- o Iron stores in BM: empty

- Mention one most important investigation at this point.

Answer:

- Transferrin level

QUESTION 8

Mention the possible causes of anemia in SLE

- o ACD
- o Iron def anemia (due to bleeding tendency)
- o HA (warm reacting)
- o Aplastic anemia (rare)
- o PA (associated autoimmune diseases)

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QUESTION 9

A 55 year old male:

Symptoms of dyspnea on exertion,
easy fatigability, and lassitude for past 2 to 3 months.
He denied hemoptysis, GI, or other bleeding.
He claimed diet was good, but appetite varied.

Hb: 7 gm %

MCV: 73 Fl,

Serum iron: ↓↓

Mention the initial investigation you would request.

Answer: Occult blood

QUESTION 10

A 57 year old male:

Seen by local physician for routine preoperative exam,
prior to dental surgery.
Found to have low hemoglobin and a huge splenomegaly.

Hb: 8 gm %

WBCs: 62,000 / cmm, with abnormal cells:

WBCs: large nucleus, with abnormal cells.

Platelets: many projections in the cytoplasm

What is the most likely diagnosis ??

Answer: Hairy cell leukemia

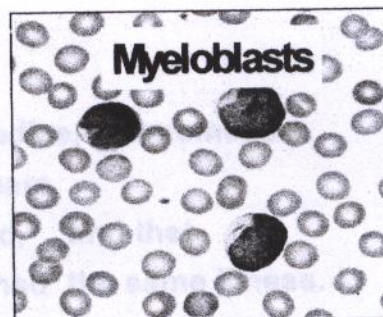
QUESTION 11

A 42 year old male:

Recurrent upper respiratory infections,
with fever, Submandibular swellings.

He noted that cuts on his hands did not heal well.

The course of his illness deteriorated very rapidly.



Hb: 10 gm %

WBCs: 71,000 / cmm, with abnormal cells.

Platelets: 51,000 / cmm

What is the most likely diagnosis ??

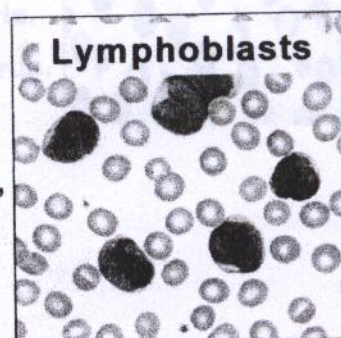
Answer: **AML**

QUESTION 12

A 6 year old male:

Recurrent upper respiratory infections with fever,
Easy bruising, bony pains.

Generalised LN, HSM, skin petichae.



Hb: 9 gm %

WBCs: 92,000 / cmm, with abnormal cells.

Platelets: 26,000 / cmm

What is the most likely diagnosis ??

Answer: **ALL**

QUESTION 13

A 19 year old female: pallor, mild jaundice, splenomegaly.

History of cholecystectomy since 10 years.

He stated he had always had "low blood," and that his father & paternal grandfather both had the same illness.

Hb: 10.8 gm %

MCV: 84.1 Fl

Retix: 7 %

Total Bil: 5.4 mg / dL

Urea: 23 mg / dL (20 – 40 mg / dL)

Mention one important investigation at this point.

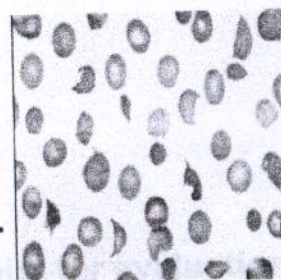
Answer: Osmotic fragility test for HS

QUESTION 14

A 32 year old female, just after her second pregnancy:

Two day history of ecchymoses, petechiae, hematuria.

She had behavioural changes, amnesia & mild icterus.



Hb: 6.6 gm %

WBCs: 7,000 / cmm

Platelets: 14,000

Total Bil: 3.2 mg / dL

Urea: 68 mg / dL (20 – 40 mg / dL)

How would you treat this lady ??

Answer: ttt of TTP (plasmapheresis + corticosteroids)

QUESTION 15

A 41 year old male.

Almost 4 years prior to admission, he was diagnosed with a brain tumor.

It was removed surgically and he received chemotherapy.

After about three years, the tumor recurred.

He was treated with radiation, and chemotherapy was resumed.

He now presented with fever, pallor & bruises.

Hb: 9.1 gm %

MCV: 68 fL

Serum iron: ?

WBCs: 2,300 / cmm

Platelets: 51,000 / cmm

What is the most probable diagnosis ??

Answer: MDS causing pancytopenia & sideroblastic anemia

QUESTION 17

A 32 year old female is referred by an oncologist for evaluation of bleeding tendency prior to LN biopsy.

Medical history reveals that she has had mild thrombocytopenia and a positive Coombs' test in the past .

She also has skin rash & arthralgia.

BT: 10 minutes, CT: 7 minutes, INR: 1

- Mention one most important investigation at this point.

What is the most important test that you should do next ?

Answer: Hb electrophoresis (Hb F of Thalassemia)

Answer: serology (SLE antibodies)

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QUESTION 18

A 78 year-old male is referred to your office with fatigue, decreasing energy, dyspnea, and a hematocrit of 24%. His past history is significant for oxygen dependant COPD, inoperable coronary artery disease and a prosthetic aortic valve replaced 8 years ago due to calcific aortic stenosis. On physical exam the patient is chronically ill. A grade 2/6 systolic ejection murmur is heard at the base of the heart, radiating to the neck. There is mild clubbing of the digits. Stool is negative for occult blood.

Mention 2 tests you would ask.

Answer: HA due to prosthetic valve

1. Retix
2. Blood film: Schistocytes

QUESTION 19

- A ♂ patient, 19 years old was investigated for his disease:

- o Hb: 9 gm %
- o Retix: 7 %
- o MCV: 73 Fl

- Mention one most important investigation at this point.

Answer: Hb electrophoresis (Hb F of Thalassemia)

QUESTION 20

Pernicious anemia is characterized by:

- o Macrocytic anemia. T
- o Pyramidal lesions. T
- o Splenomegaly. T
- o Deep sensory loss. T
- o Cerebellar ataxia. F

QUESTION 21

Hemolytic anemia is a complication of:

- o Prosthetic heart valves. T
- o Mycoplasma pneumonia. T
- o Megaloblastic anemia. T
- o Malarial infection. T
- o Sulphonamide therapy. T

QUESTION 22

Hemorrhagic disorders due to ? clotting factors:

- o Hereditary hemorrhagic telangiectasia. F
- o Christmas disease. T
- o Senile purpura. F
- o Henoch- Schönlein purpura. F
- o Hemophilia. T

QUESTION 23

Typical features of ITP include:

- o IgG – mediated thrombocytopenia. T
- o Predominantly affects patients > 60 years old. F
- o Prolongation of the bleeding time. T
- o Palpable splenomegaly. F
- o Response to corticosteroid therapy. T

QUESTION 24

DIC is a complication of:

- o Amniotic fluid embolism. T
- o Incompatible blood transfusion. T
- o Hypovolemic & anaphylactic shock. T
- o Septic shock. T
- o Carcinomatosis. T

QUESTION 25

- **A ♀ patient, 21 years old was investigated for stroke:**

- o Hb: 8 gm %
- o Retix: 12 %
- o MCV: 92 Fl
- o WBCs: 2500 / cmm
- o Platelets: 80,000 / cmm

- **Mention one most important investigation at this point.**

Answer: Flow cytometry for PNH

QUESTION 26

A male patient 17 years old
presented to the hospital with
general manifestations of hemolytic anemia
associated with dark coloured urine

Enumerate the different possibilities

Answer:

Hemolytic crisis
Intravascular hemolysis
Complicated by OJ

QUESTION 29

Mention the CBC of a patient with Addison's disease

QUESTION 27

- A ♂ patient, 34 years old was investigated for his disease:
 - o Hb: 6 gm %
 - o WBCs: 5,000 / cmm
 - o BLASTS
- What is the most probable diagnosis ??
- Mention 2 important investigations at this point.

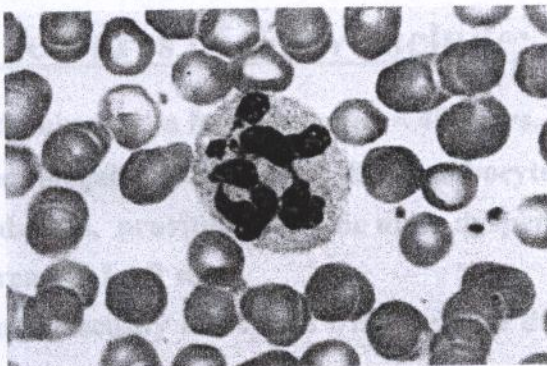
Answer:

Cytochemistry
BM examination

Answer: Refer to the notes

QUESTION 28

Mention the disease that caused this blood film



Answer: Megaloblastic anemia

QUESTION 29

Mention the CBC of a patient with Addison's disease

Answer:

Increased: Lymphocytes, Basophils, Eosinophils

Decreased: RBCs, Neutrophils

Maybe: CBC of pernicious anemia

QUESTION 30

Give reasons for:

- o ACD.
- o Anemia in CLL.
- o Need for parenteral iron in IDA.
- o Thrombosis in PRV.
- o ARF in DIC.

Answer: Refer to the notes

QUESTION 31

Typical features of PRV include:

- a) Predominance in females aged < 40 years. F
- b) Splenomegaly, leukocytosis & thrombocytosis. T
- c) Headaches, pruritus & peptic ulcer dyspepsia. T
- d) Decreased LAP score. F
- e) ↑ blood viscosity associated with vascular disease. T

QUESTION 32

Typical features of CLL include:

- a) Onset in younger patients than CML. F
- b) Development of AIHA. T
- c) Presentation with massive HSM & anemia. F
- d) LN associated with recurrent infections. T
- e) Lymphoblasts in peripheral blood. F

QUESTION 33

Causes of thrombocytosis include:

- a) MPDs. T
- b) Hypersplenism. F
- c) Carcinomatosis. T
- d) Connective tissue disorders. T
- e) Bleeding. T

Answer: Refer to the notes

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QUESTION 34

Features of DIC include:

- a) Thrombocytopenia.
- b) Schistocytes in the peripheral blood.
- c) ↓ serum fibrin degradation products.
- d) Normal PT & normal TT.
- e) Prolongation of the APTT.

T
T
T
F
T

QUESTION 35

Mention the possible causes of anemia in cancer stomach

Answer:

Iron deficiency anemia
Megaloblastic anemia
ACD
Myelophthistic anemia
Sideroblastic anemia
Pernicious anemia
Acute post – hemorrhagic anemia

QUESTION 36

Give reasons for:

- o Anemia in myxoedema.
- o Anemia in renal failure.
- o Thrombosis & bleeding in PNH.
- o Stroke in PRV.
- o Bleeding in DIC.

Answer: Refer to the notes

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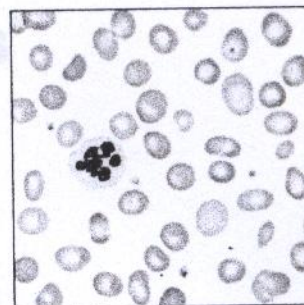
QUESTION 37

A 37 year old female, alcoholic.

Lifelong history of a seizure disorder, treated since age two.

She was always advised to quit alcohol because of her seizures.

At a routine check with his neurologist, he complained of fatigue, exertional dyspnea, and lightheadedness over the past 2-3 months.



Hb: 8.7 gm %
 MCV: 112 fL
 Serum iron: ↑
 Blood film: see the following

What is the your initial test ??

Answer:

Serum folic acid (alcoholic, use of anti – epileptic drugs)

A) Platelet defect

QUESTION 38

A 43 year old female.

History of fibrocystic breast disease.

Seen for routine work-up prior to breast biopsy.

Moderate splenomegaly, no other organomegaly.

Hb: 11.7 gm %
 WBCs: 133,000 / cmm
 Platelets: 317,000 / cmm

What is the your initial test ??

How would you confirm your diagnosis ??

Answer: CML

(LAP for CML, to say whether it is CML

or CLL which is not likely because of age)...not acute leukemia bec
 it is rather not aggressive (discovered accidentally)

Confirm by: BM

Acute phase reactants

- Increase in response to injury
- Useful markers of inflammation

CRP, Leukocytosis, ESR

Ferritin

Platelets

Fibrinogen

Haptoglobin

vWF

Ceruloplasmin

Alpha 1 antitrypsin

Drug – induced purpura

A) Platelet defect

1. Thrombocytopenia:

a) Decreased platelet production:

- BM failure (aplastic anemia): drugs causing aplastic anemia.
- Megaloblastic anemia:
 1. Drugs that lower folic acid (..... &)
 2. Drugs that cause general malabsorption:
Cholestyramine, Neomycin, Dendivan
- MDS: Chemotherapeutic drugs

b) Increased platelet destruction:

- Autoimmune: drugs causing AIHA & drugs causing SLE.

2. Thrombocytopathy:

- Antiplatelet drugs: aspirin, dipyridamole, ticlopidine.
- Autoimmune: drugs causing SLE

B) Vessel wall defect

Vascular Purpura

- Salicylates, Sulphonamides, Penicillin, Corticosteroids.

Imaging in blood diseases

Iron deficiency anemia:

PNH

Thalassemia

Sickle cell anemia

Aplastic anemia

Acute leukemias

CML

Idiopathic myelofibrosis

(Stem cell transplantation)

Lymphoma:

- Abdomen:

(Abdominal ultrasonography & CT)

- Chest:

(CXR & CT)

Hypersplenism:

Complications of BMT

Infections (Bacterial, fungal, Viral (CMV, HSV))

Graft failure

Hemorrhagic cystitis (Cyclophosphamide)

Veno – occlusive dis (Cyclophosphamide)

Relapse of the original disease

Imaging in blood diseases

Iron deficiency anemia:

- To detect GIT hemorrhage:
(Ba studies, Angiography, radio-isotope bleeding scan)
- Ba swallow:
Post-cricoid web in Plummer Vinson syndrome

Hemolytic anemia:

- To measure life span of RBCs:
(Cr - labelled RBCs)
- X - ray for Thalassemia:
(Skull, long bones)

Lymphoma:

- Abdomen:
(Abdominal ultrasonography & CT)
- Chest:
(CXR & CT)

Hypersplenism:

1. What is the life span of RBCs?
2. What is the life span of RBCs?
3. How to detect splenomegaly?
4. Specify the life span of RBCs in the UL & in the LL.
5. Enumerate the risk factors in this patient.
6. What is the laboratory investigation you would ask for this patient?

The patient was admitted to hospital where general & specific treatment was started.

He stayed in hospital for 4 weeks & was then discharged. He was advised to come for follow up after 2 months.

7. Describe the general care that this patient should receive in hospital.
8. Would you give anticoagulants in this case?
9. Mention the most important 2 lines of treatment in this patient.
10. What are the neurological changes you expect to find on follow up?

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